FULL PROTOCOL TITLE OF THE STUDY

Implementation of Comprehensive Geriatric Assessment based perioperative medicine services to improve clinical outcomes for older patients undergoing elective and emergency surgery with cost effectiveness

SHORT STUDY TITLE and ACRONYM

Perioperative medicine for older people undergoing surgery scale up (POPS-SUp)

Chief Investigator:

Professor Jugdeep Dhesi

Sponsored by:

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Name and address of Co-Investigator(s), Trial Manager and key study contacts, Funder, Statistician, Laboratories etc.

Name:	Professor Jugdeep DHESI (CI)
Address:	Older Person's Assessment Unit, Ground Floor, Bermondsey Wing, Guy's Hospital, London SE1 9RT
Telephone:	07525451329
Email:	Jugdeep.dhesi@gstt.nhs.uk pops-sup@contacts.bham.ac.uk (study email)

Name:	NIHR
Address:	Alpha House, Enterprise Road Southampton SO16 7NS
Telephone:	02380597558
Email:	cheryl.baker@nihr.ac.uk

Name:	Laura MAGILL
Address:	Birmingham Centre for Observational and Prospective Studies (BiCOPS) University of Birmingham Clinical Trials Unit
Telephone:	01213715888
Email:	E.L.Magill@bham.ac.uk>

Name:	Professor John NORRIE (statistician)
Address:	University of Belfast
Telephone:	0131 6519916
Email:	j.norrie@ed.ac.uk

Name:	Dr Andy HEALEY (health economist)
Address:	David Goldberg Centre, 18 De Crespigny Park, London SE5 8AF
Telephone:	02078480878
Email:	andy.healey@kcl.ac.uk

Name:	Professor Cecilia VINDROLA (process evaluation)
Address:	University College London, Charles Bell House 43-45 Foley Street, Department of Targeted Intervention, London W1W 7TY
Telephone:	02077692000
Email:	c.vindrola@ucl.ac.uk

PROTOCOL VERSION NUMBER AND DATE

Version Stage	Versions No	Version Date	Protocol updated & finalised by;	Detail the key protocol update
Current	*1.0*	*09.08.2024*	*Professor J Dhesi*	
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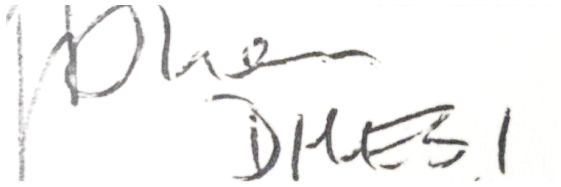
SIGNATURE PAGE

The Chief Investigator and the R&D (sponsor office) have reviewed this protocol. The investigators agree to perform the investigations and to abide by this protocol
The investigator agrees to conduct the trial in compliance with the approved protocol, EU GCP, the UK Data Protection Act (2018), the Trust Information Governance Policy (or other local equivalent), the UK policy Framework for Health and Social Care research, the Sponsor's SOPs, and other regulatory requirements as amended.

Chief investigator



Signature Date 09.08.24

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1. LIST OF ABBREVIATIONS AND DEFINITIONS

AE	Adverse Event
AR	Adverse Reaction
ASR	Annual Safety Report
CA	Competent Authority
CI	Chief Investigator - The overall lead researcher for a research project (Outside the UK the term Coordinating Investigator or Investigator may be used). Chief investigators are responsible for the overall conduct of a research project.
CGA	Comprehensive Geriatric Assessment and optimisation
CRF	Case Report Form
CRO	Contract Research Organisation
GAfREC	Governance Arrangements for NHS Research Ethics Committees
HES	Hospital Episode Statistics
ICF	Informed Consent Form
Main REC	Main Research Ethics Committee
NHS R&D	National Health Service Research & Development
POPS	Perioperative medicine for Older People undergoing Surgery
PI	Principal Investigator- An individual responsible for the conduct of the research at a research site. There should be one PI for each research site. In the case of a single-site study, the chief investigator and the PI will normally be the same person.
QA	Quality Assurance
QC	Quality Control
Participant	An individual who takes part in a clinical trial or in this case the participant is a hospital site
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedure
Sponsor	The organisation or partnership that takes on overall responsibility for proportionate, effective arrangements being in place to set up, run and report a research project.
SSA	Site Specific Assessment
SMG	Study Management Group
SSC	Study Steering Committee

2. SUMMARY/SYNOPSIS

Title	Implementation of Comprehensive Geriatric Assessment based perioperative medicine services to improve clinical outcomes for older patients undergoing elective and emergency surgery with cost effectiveness
Protocol Short Title/Acronym	Perioperative medicine for Older People undergoing Surgery Scale Up (POPS-SUp)
IRAS Number	335587
REC Reference	
EDGE reference	150947
Study Duration	39months
Health condition(s) or problem(s) studied	Frailty, multimorbidity, cognitive impairment and decision making in the perioperative setting. Implementation of perioperative medicine services to address these issues in patients undergoing elective and emergency surgery
Primary objective	Can CGA-based perioperative medicine services (POPS services) be implemented throughout the NHS, to improve clinical outcomes for older patients undergoing elective and emergency surgery with cost effectiveness?
Secondary objective (s)	To determine if systematic implementation of POPS services using a predefined trimodal implementation strategy, at scale across NHS hospitals, can result in: •successful and sustainable implementation of POPS services across the NHS •improved clinical outcomes for patients undergoing elective and/or emergency surgery •cost effective perioperative care
End of study definition	HES linkage and data analysis
Number of Participants	114 consented NHS staff participants 216 consented patient/carer/family member participants 2,500 non-consented patient participants (routine clinical data recorded with CAG permission)
Study Type	A hybrid implementation-effectiveness interrupted time series study using mixed-methods
Data collected/storage (if applicable)	The data will be collected and stored by the research group

3. INTRODUCTION

Two thirds of elective and two fifths of emergency surgical procedures in the NHS are undertaken in people aged over 65 years [1]. Surgery offers definitive management of many age-related diseases, relieving symptoms and extending life. These benefits are weighed against the risk of adverse outcomes. Age-related physiological decline, multimorbidity, frailty and dementia predispose older people to postoperative medical complications e.g. pneumonia, acute kidney injury and delirium [2,3]. These complications result in higher postoperative mortality, slower and incomplete functional recovery, poorer experience and higher NHS resource use by older people [4]. Age-related conditions can be identified and modified using Comprehensive Geriatric Assessment and optimisation (CGA). This holistic process involves clinical skills and standardised tools to assess medical, functional, psychological and social domains prompting individualised evidence-based interventions, e.g. preoperative optimisation of hypertension or anaemia; medicines modification to reduce delirium or falls; better-informed shared decision making; anticipation and provision of rehabilitation; and early home adaptations [5]. Level 1 evidence demonstrates that older people receiving CGA during an acute medical admission are more likely to be alive and living at home at one year [6]. Likewise, CGA cost-effectively reduces morbidity and mortality after elective or emergency surgery, increasing the likelihood of discharge home [7,8,9,10]. National organisations advocate CGA-based services for older patients undergoing elective and emergency surgery [11,12,13].

Some hospitals have established CGA-based Perioperative medicine for Older People undergoing Surgery (POPS) services but others have been unsuccessful [14]. This results in unacceptable variation in access to and quality of care for high-risk, older surgical patients across the NHS, leading to unnecessary deaths, complications and NHS costs [13,15]. The challenges to systematic scale up of complex interventions (such as POPS services) include a heterogeneous patient population, multiprofessional stakeholders, need to ensure fidelity to the intended intervention and failure to adapt the intervention to the local context [16]. Overcoming barriers to NHS scale up of complex interventions, such as POPS services, requires a systematically codesigned implementation strategy [16,17]. POPS-SUp will investigate two inter-linked interventions. First, an implementation strategy designed to support implementation of POPS services and second, the clinical and cost effectiveness of POPS services established using that implementation strategy to deliver perioperative CGA-based care.

POPS-SUp, a hybrid implementation-effectiveness study, will examine whether CGA-based perioperative medicine services (POPS) can be implemented throughout the NHS to improve clinical outcomes for older patients undergoing elective or emergency surgery with cost effectiveness for the NHS.

<u>Brief review of the evidence on CGA-based POPS services in the perioperative setting</u>

Evidence supporting effectiveness of CGA-based POPS services

Age-related factors (physiological decline, multimorbidity and frailty) predict adverse postoperative outcomes [2,3]. Level 1 evidence supports the use of CGA as a multidomain process that identifies and treats these age-related factors to reduce postoperative morbidity and mortality, and improve rates of return to usual residence after surgery, with cost effectiveness [7,8,9]. These clinical and economic benefits have been demonstrated in elective and emergency surgical settings [7,8,9,10]. By necessity, in emergency surgery, CGA is tailored to the time available preoperatively and delivered postoperatively. The benefits of perioperative CGA can be attributed to a systematic approach to making new diagnoses, stopping/starting/optimising medications, supporting healthy behaviours, informing shared decision making (i.e. is surgery right for this person), anticipating and mitigating postoperative complications, and supporting timely rehabilitation and discharge planning

[18]. This CGA approach is broader than 'prehabilitation programmes', which aim to improve 'fitness for surgery' by offering advice on smoking and alcohol cessation, exercise and psychological interventions. Such programmes do not provide multidomain assessment and optimisation, with limited evidence of improved postoperative outcomes in older people in contrast to CGA [19,20,21].

Evidence supporting implementation of CGA-based POPS services
Surveys and national audit have shown an increase in establishment of POPS services over the last seven years with consistent clinical outcomes seen in large teaching hospitals, smaller district general hospitals and internationally in comparable healthcare systems [13,14,22,23]. Successfully established services have been developed using a published POPS logic model [24]. However, the majority of NHS hospitals have not yet embedded POPS services into routine care, as implementation of complex interventions like POPS remains challenging.

Prior effectiveness-implementation studies inform this proposal. The NIHR funded HoW-CGA study was unsuccessful in delivering perioperative CGA using a toolkit. The main limitations were content, face validity and usability of the toolkit, and lack of a clearly defined strategy to overcome behavioural and cultural barriers during implementation [25]. Similarly, the EPOCH study reported no impact on 90 day mortality or hospital length of stay after implementation of a care pathway for patients undergoing emergency abdominal surgery. Despite delivery of the pathway as planned at cluster level, fidelity to the intervention at hospital level was variable due to insufficient engagement of professionals and lack of recognition of necessary time and organisational resource required [26]. Building on and learning from this work, POPS-SUp aims to address these implementation challenges, through use of the MRC framework for developing and evaluating complex interventions [27], the ADAPT framework [28] and our extensive preparatory and pilot work.

4. PATIENT AND PUBLIC INVOLVEMENT

The POPS-SUp team have conducted extensive PPIE work in the piloting and set up of POPS-SUp which informed the funding application and design of the study. This PPIE work has been undertaken with three groups;
[1] patients and their carers/family members
[2] community of practice – clinical and managerial professional stakeholders involved in the pilot work undertaken with NHS elect which informed POPS-SUp
[3] professional stakeholder organisations

All three groups have expressed an urgency to undertake the POPS-SUp study which they believe will address many of the challenges in perioperative care in the post pandemic era. In particular, patients told us POPS services will help them prepare for surgery, support them with decision making and recover from surgery more quickly and in their preferred place. Professional organisations emphasised the need to scale up POPS services at pace to reduce geographical variation in perioperative care for older patients. Since 2017, through open days, workshops and media events, public and professional partners have co-developed the study aim, design, ethical considerations, outcome measures and dissemination strategy.

Public involvement continues to be central to POPS-SUp. We intend to ensure diversity and equality of opportunity enabling active involvement in this research. We will draw on NIHR definitions where inclusion means taking deliberate action to meet the needs of different people and promote environments where everyone is respected, valued for who they are and able to achieve their full potential. NIHR define diversity as understanding everyone is unique, respecting and valuing all forms of difference. We will draw on guidance from the INCLUDE project and NIHR Race equality Framework to inform our practice.

All patient, public involvement and engagement (PPI/E) activity will be led by the Accountable Academic Lead and public advisor, coordinated by the study manager. Our leadership team will be responsible for oversight and planning of PPI/E in research, impact, reaching hidden communities, diversity and race equality, organising research training to public advisors, if required. Training in cultural competency and inclusive practices will be offered to all advisory group members. Two public advisors with lived experience will contribute to study management and independent oversight committee with allocated budget.

Based on communication with NIHR our PPIE strategy will use three stakeholder groups who work with us throughout the study. Induction, training, support and coaching will be offered.

[a]Public advisory group 8-10 patients/carers with lived experience from ethnically diverse communities, range of genders and localities.
[b]Community of practice/network comprising clinicians delivering NHS POPS services
[c]Multidisciplinary professional stakeholder group: clinicians, professional bodies, charity representatives, decision makers.

Our stakeholder groups will input into all aspects of POPS-SUp including regular review of progress of the study, documentation development and review, planning and delivery of end of research meetings and writing of public facing material (e.g. abstracts for dissemination). We will encourage our PPI/E advisors to present at these meetings, with support from research staff and they will help develop conference material. We will work with our public advisory chair and our public advisory group to produce lay summaries for patient publications in a variety of formats.
Effective communication between stakeholder groups and the research team is fundamental to the success of this project. Accountable Academic Lead for PPIE and our public advisor will be responsible for ensuring strong links between the stakeholder groups and research team are maintained. At appropriate stages of the programme, coinvestigators and programme staff will be invited to attend relevant stakeholder meetings to present their planned work, share study material (e.g. draft participant information leaflets, draft questionnaires) and present results.
The groups will meet at the outset of POPS-SUp and 6 monthly. All materials will be provided ahead of the meetings to allow members to read and consider the materials and prepare any questions for the research team. Virtual methods will be used to support inclusion. Digital exclusion will be mitigated by providing data packages, technical support or offering the option to attend meetings in-person in one of the participating sites. Appropriate budget has been included in this bid to support all stakeholder and public involvement and engagement activities, including dissemination. We will report our public and patient involvement in research using the GRIPP2 checklists.

5. TRIAL OBJECTIVES AND PURPOSE

Research question
Can CGA-based perioperative medicine services (POPS services) be implemented throughout the NHS, to improve clinical outcomes for older patients undergoing elective and emergency surgery with cost effectiveness?
Aim
To evaluate implementation, clinical and cost effectiveness of POPS services for older patients undergoing elective and emergency surgery

Objectives
To determine if systematic implementation of POPS services using a predefined trimodal implementation strategy, at scale across NHS hospitals can result in
•successful and sustainable implementation of POPS services across the NHS

•improved clinical outcomes for patients undergoing elective and/or emergency surgery
•cost effective perioperative care

6. STUDY DESIGN & FLOWCHART

6.1 Study Design

POPS-SUp is a hybrid implementation-effectiveness interrupted time series study using mixed-methods to examine the use of a coproduced implementation strategy, to support implementation of POPS services and evaluate clinical and cost effectiveness across the NHS. Evaluation will use mixed qualitative and quantitative methods, through embedded process evaluation, quantitative evaluation of clinical and cost effectiveness and qualitative appraisal of patient and staff experience. POPS-SUp will examine two inter-linked interventions:

- The first intervention is a trimodal implementation strategy designed to support implementation of POPS services
- The second intervention is the POPS service delivering perioperative CGA-based care

<u>The implementation strategy</u>
The trimodal POPS implementation strategy uses a toolkit, quality improvement coaching and mentoring, and training in the use of data and measurement to deliver improvement. The toolkit includes clinical resources, education and training and business resources.

NHS Elect will support the delivery of this implementation strategy through structured, online meetings between participating hospital site teams and expert coaches (with expertise in clinical POPS services, improvement science and data management). The NHS Elect POPS programme will include an initial site visit, two-weekly team meetings, monthly events for the cohort and regular webinars. POPS-SUp will study the impact of this co-produced implementation strategy on implementation outcomes.

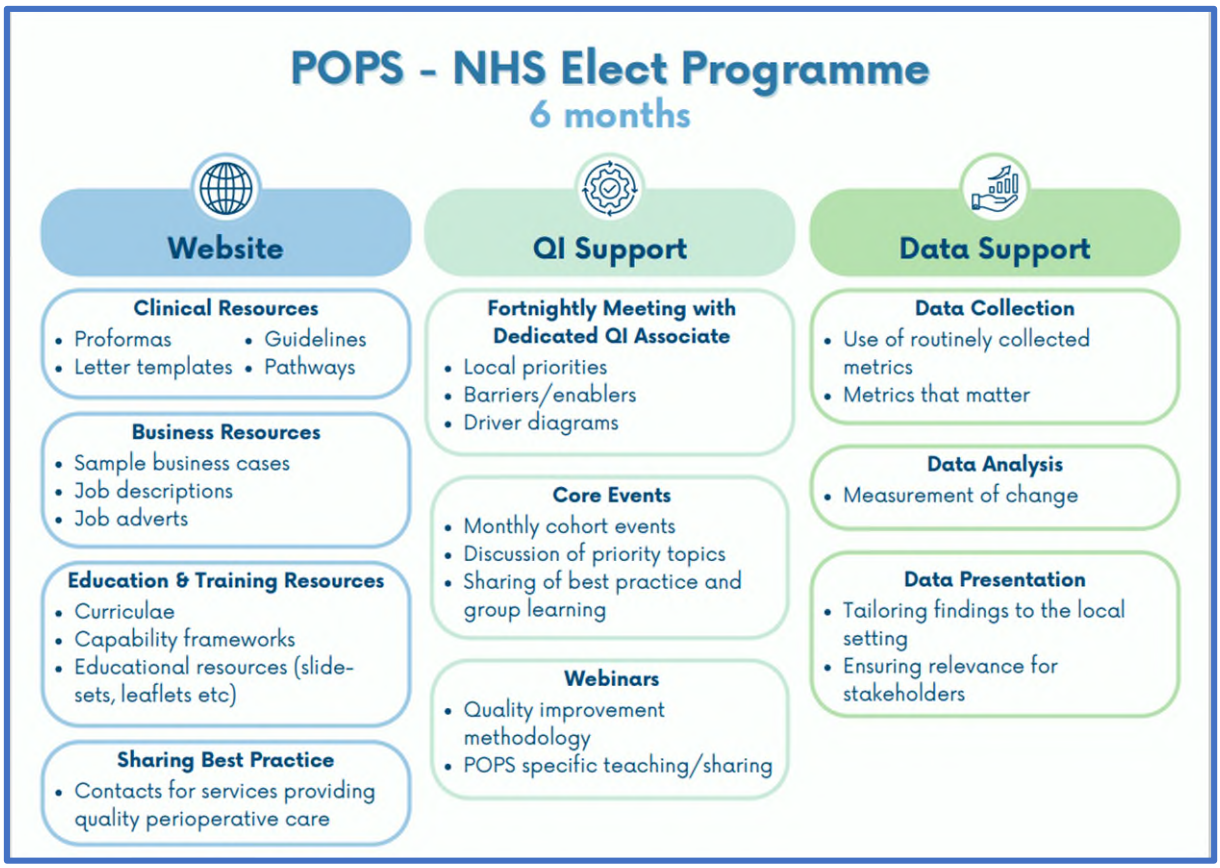

Figure 1 – NHS Elect implementation strategy

Perioperative CGA-based care delivered through a POPS service

The POPS services to be evaluated in POPS-SUp use Comprehensive Geriatric Assessment and optimisation (CGA) methodology. CGA involves a holistic assessment of a patient across medical, functional, social and psychological domains, using objective measures to inform multidisciplinary optimisation. The POPS service, using CGA methodology at each of the eighteen participating hospitals, will be delivered by a geriatrician-led multidisciplinary team from that hospital, supported by the trimodal NHS Elect POPS implementation strategy. All patients under the care of general and/or orthopaedic and/or urological and /or vascular surgery teams at all study sites will receive perioperative care delivered through the planned intervention, namely the POPS service implemented through the trimodal implementation strategy, supported by the NHS Elect POPS programme. The POPS service will deliver perioperative care for patients living with frailty, multimorbidity, cognitive issues and/or those in whom the decision to operate is not clear, who are being considered for major emergency and/or elective general and/or orthopaedic and/or urological and /or vascular surgery.

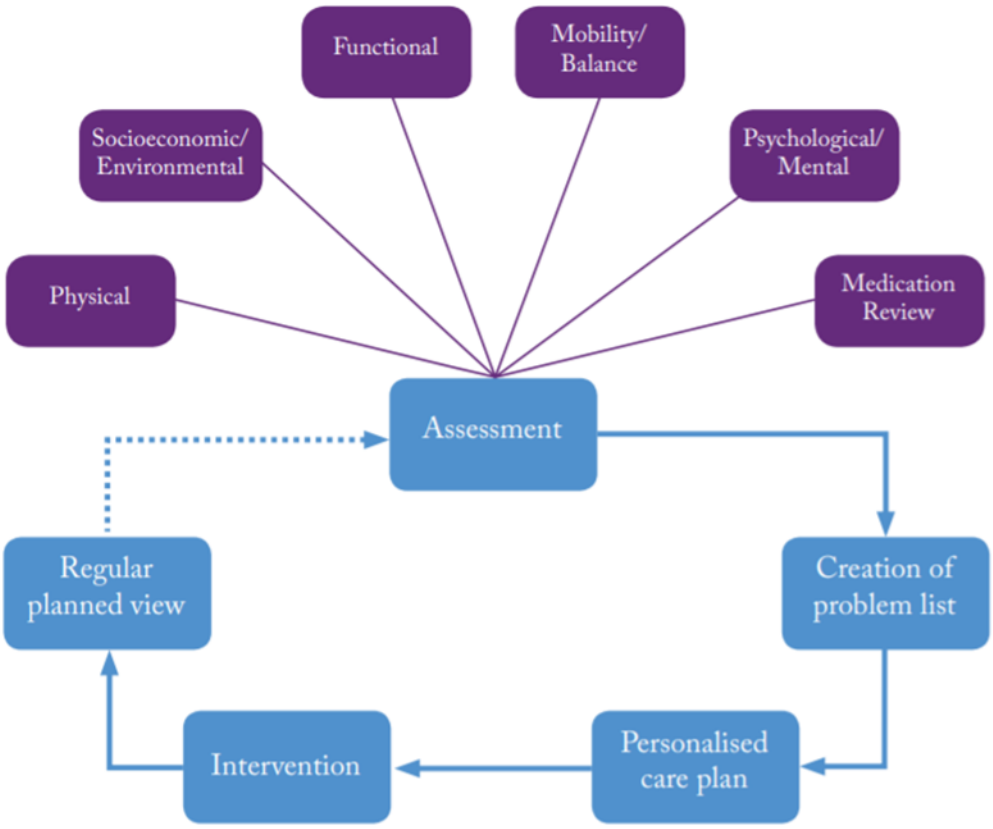

Figure 2 – Comprehensive Geriatric Assessment

Coprimary outcomes

In keeping with the MRC framework for complex interventions, POPS-SUp will use coprimary outcomes.

These coprimary outcomes are:

- Reach to assess implementation

Reach – no. patients seen by POPS / no. of patients eligible for POPS review

This will be defined according to which surgical specialty the service is being established in e.g. EGS/Urology etc and which patients will be seen e.g. >65 years / frailty CFS 5 / multimorbidity etc. It might be different between sites.

-Length of hospital stay in days to assess clinical and cost effectiveness.

Secondary implementation outcomes include:

-fidelity to clinical components of perioperative CGA

This will be case note review of all patients seen by the POPS services to establish fidelity to the core components checklist for CGA

-fidelity to core components of POPS services

This will be measured against POPS logic model core components which will be adjusted according to the service being established eg some teams may not be providing postoperative care

Will be measured through process evaluation ie staff members will be interviewed/ observed/ surveys.

- Acceptability and feasibility of the implementation strategy will be assessed through process evaluation.

Acceptability – staff and patient interviews - through process evaluation

Feasibility – staff and patient interviews in addition to questions on how long does clinic take / is there enough space / sufficient staff etc - through process evaluation

Secondary effectiveness outcomes include:
-30day readmission (HES linkage)
-Postoperative complications (Postoperative Morbidity Score) collected on postoperative/post-admission days 3 and 5
-Postoperative delirium recorded through POMS and 4AT on days 3 and 5 and through retrospective notes review
-Same day cancellation
-Return to preoperative place of residence (clinical record)
-Days alive and out of hospital 90 days (HES linkage)
-90 day and 12 month mortality (HES linkage)
-Operative or non-operative management
Was the initially suggested procedure undertaken or did the patient undergo a different or no procedure?
- Clinician defined, 'medically fit for discharge'
Notes review at or after discharge
- HRQoL(EQ-5D-5L) (collected in a consented subgroup of patients) to be collected in the preimplementation and in postimplementation phase
-Shared decision making (SDMQ9) (collected in a purposively sampled consented subgroup of patients) to be collected in the preimplementation and in postimplementation phase
-Decisional regret (Decision Regret Scale) (collected in a purposively sampled consented subgroup of patients) to be collected in the preimplementation and in postimplementation phase
(6 patients per site to be consented in each of the pre and post implementation phases across 18 sites. Purposive sampling to include elective/emergency, surgery/no surgery and LoS</> 5 days. Applies to SDMQ9 and DRS. Estimated total 216 patients)

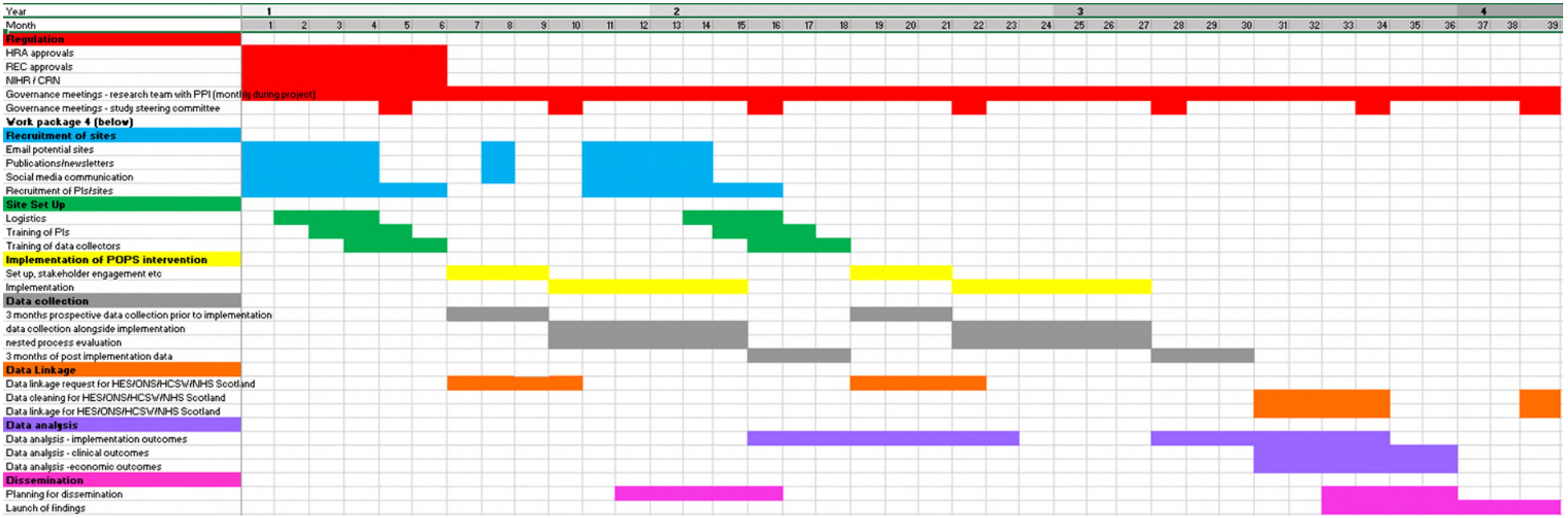

Figure 3: Study Gantt chart

7. PARTICIPANT SELECTION

- Eighteen hospitals (two sequential cohorts of nine hospitals) providing general and/or orthopaedic and/or urological and/or vascular surgery located across England, Scotland, Wales and Northern Ireland, with representation of rural and urban NHS services, serving diverse populations in terms of socioeconomic circumstances, race and ethnicity will be selected to deliver the study. These sites will be required to have a geriatrician (consultant, speciality and specialist doctors, SAS) with allocated time to support implementation and support from a hospital executive board member.

Participants

(i) NHS staff at the eighteen sites implementing POPS services, including includes geriatricians, anaesthetists, surgeons, nursing and allied health professionals, and managers

(ii) Patients aged over 50 years under the care of general and/or orthopaedic and/or urological and /or vascular surgeons

(iii) Carers/family members closely involved in the care of patients aged over 50 years under the care of general and/or orthopaedic and/or urological and /or vascular surgeons (some of these carers/family members will be related to patient participants from [ii] and others may be related to patients who do not display capacity to consent to the study)

7.1 Participant inclusion criteria

Our inclusion and exclusion criteria at hospital site level are designed to maximise participation by hospitals regardless of geography, type of hospital, patient population or resources. Recruitment at hospital site level aims to ensure participation of patients often underrepresented in research; those living with frailty, living in care homes, lacking capacity to consent, those who do not speak English, those with sensory impairments.

(i) Inclusion criteria at NHS staff level:

NHS staff employed at the participating site involved in implementation of POPS intervention and/or delivery of perioperative care

(ii & iii) Inclusion criteria at patient level (non-consented and consented groups):

Patients aged over 50 years under the care of general and/or orthopaedic and/or urological and /or vascular surgical care at participating hospitals

(iiii) Carer/family member closely involved in the care of patients aged over 50 years under the care of general and/or orthopaedic and/or urological and /or vascular surgeons

7.2 Participant exclusion criteria

(i) Exclusion criteria at NHS staff level - none

(ii) Exclusion criteria at patient participant level (non-consented) -none

(iii) Exclusion criteria at patient participant level (consented)

- Prisoners
- Dementia or delirium so severe as to preclude completion of Shared Decision Making Q9/EQ 5D 5L / Decisional regret scale / No capacity to consent to study

(iiii) Exclusion criteria at carer/family member level

- carer/family member who is only distantly involved in the care of patients aged over 50 years under the care of general and/or orthopaedic and/or urological and /or vascular surgeons

8. STUDY PROCEDURES

Chronological summary of study procedures;

Research activity	**Detail of research activity**	**Approached by**	**Undertaken by**
Site recruited /opened	Initial contact with potential site	POPS-SUp CI	POPS-SUp CI
	Information provision to local PI	POPS-SUp CI	POPS-SUp CI
	Site initiation visit		POPS-SUp CI, POPS-SUp Fellow and NHS Elect team
	Promotion of study at local site to staff and patients		Local PI and clinical/research team at participating site
Pre-implementation data collection *Months 1-3*	Clinical data collection through review of patient notes (national opt-out checked) *(This activity may be completed retrospectively in order to deliver POPS-SUp on time and to budget)*		Local PI and clinical/research team at participating site
	Patient interview/questionnaires (written consent)	Local PI and clinical team	Local PI and clinical/research team at participating site and research team (process evaluation)
	Carer/family interview/ questionnaires (written consent)	Local PI and clinical team	Local PI and clinical/research team at participating site and research team (process evaluation)
	Staff interview and diary (written consent)	Local PI and clinical team	Research team (process evaluation)

Implementation data collection *Months 4-9*	Clinical data collection through review of patient notes (national opt-out checked)		Local PI and clinical/research team at participating site
	Patient interview/questionnaires (written consent)	Local PI and clinical team	Local PI and clinical/research team at participating site and research team (process evaluation)
	Carer/family interview/ questionnaires (written consent)	Local PI and clinical team	Local PI and clinical/research team at participating site and research team (process evaluation)
	Staff interview and diary (written consent)	Local PI and clinical team	Research team (process evaluation)
	Observation of clinical POPS service (verbal consent)	Local PI and clinical team	Research team (process evaluation)
	Observation of staff/stakeholder meetings and NHS Elect meetings (verbal consent)	Local PI and clinical team	Research team (process evaluation)
Post implementation data collection *Months 10-12*	Clinical data collection through review of patient notes (national opt-out checked)		Local PI and clinical/research team at participating site
	Patient interview/questionnaires (written consent)	Local PI and clinical team	Local PI and clinical/research team at participating site and research team (process evaluation)
	Carer/family interview/ questionnaires(written consent)	Local PI and clinical team	Local PI and clinical/research team at participating site and research team (process evaluation)
	Staff interview and diary (written consent)	Local PI and clinical team	Research team (process evaluation)
HES linkage *Month 12*			Research team

Table 1 - Chronological summary of study procedures

8.1 Participant recruitment

Identification and sampling of NHS staff

The local PI will purposively identify a spread of clinicians from different disciplines and specialities and managers involved in the implementation of the POPS service.

Approach and recruitment of NHS staff
Staff will be made aware of POPS-SUp through posters, verbal communication and participant information sheet.

For the ethnographic observations the poster/leaflet and PIS will be circulated to relevant clinical and managerial staff before study launch for general information and introduction. The poster/leaflet and PIS will give staff information on the background and purpose of the evaluation, how collected data will be anonymised, and will explain the opportunity for members to opt out of any observation.

Where ethnographic observations are being conducted at NHS Elect meetings the poster/leaflet and PIS will also be circulated to all members with the meeting papers; this will re-iterate the study details and will give another opportunity for members to opt out of the observation. The poster/leaflet and PIS will also be available at the beginning of the meeting in handout form.

For all aspects of the ethnographic observations staff will be approached by researchers and verbally consented. If a member declines consent, they will not be observed and/or their contributions to the meeting will not be recorded in the field notes. We perceive the risk for participants to be low.

For the interviews and diary, staff will be approached by the local PI and clinical team and provided with the PIS via email or directly. They will have the opportunity to ask questions and have these answered by the research team. Potential participants will be given up to 24hours to consider participation in this aspect of the study after which written consent will be sought. Written consent for participation in staff interviews will be obtained by researchers. This will either be taken in person at participating sites or remotely with the consent form emailed back to the research team prior to the interview (considering the typing of names and initials as proof of consent).

Identification and sampling of patients/carers/family members
POPS-SUp intervention will be implemented at hospital site as opposed to at individual patient level. We therefore aim to collect patient metrics from routinely available data for all service users (n=2,500). We will seek CAG approval for this to be carried out without consent being sought from patients. We will however ensure that the national opt-out is checked (please see section 8.3 for details on how we will do this). In addition, the posters/leaflets raising awareness of POPS-SUp clearly state that patients can opt out of the study at any point and provide details for how to inform the research team if they wish to opt out.

In a subset of patients informed consent will allow qualitative and quantitative evaluation of satisfaction of care delivered through POPS service, satisfaction with shared decision making, decisional regret and quality of life data for health economic evaluation (n=216). A purposive sampling strategy will aim to recruit patients with a range of experiences of the surgical pathway with clinical teams identifying patients with a short and long length of hospital stay, those with and without postoperative complications, those undergoing surgery or conservative management. These patients will be identified prospectively by the clinical team from surgical wards and clinics. Patients without capacity to consent will not be recruited for this subgroup analysis. We will also purposively sample carers/family members of patients aged over 50 years under the care of general and/or orthopaedic and/or urological and /or vascular surgeons, closely and regularly involved in the care of patients including those patients who have cognitive impairment, dementia or delirium impairing capacity to consent.

Approach and recruitment of consented patients
Patients will be approached by the local clinical teams. Those who wish to know more will be provided with POPS-SUp study information. Potential participants will be given the opportunity to ask any questions they may have and have these answered by the research team. If keen to participate after provision of information written consent will be obtained in person by either clinical or research staff within 24 hours (either by local clinical teams or researchers).

Approach and recruitment of consented carers/family members
Carers/family members will be approached by the local clinical teams. Those who wish to know more will be provided with POPS-SUp study information. Potential participants will be given the opportunity to ask any questions they may have and have these answers by the research team. If keen to participate after provision of information written consent will be obtained in person within 24 hours (either by local clinical teams or researchers).

8.2 Studies where consent is not being obtained

This study is testing whether an evidence-based methodology (CGA and optimisation) can be clinically and cost effectively implemented in the perioperative setting across 18 NHS hospital sites. Patients will be cared for through the POPS services when they are considered for general and/or orthopaedic and/or urological and /or vascular surgery at participating sites.

Patient participants
Routinely obtained clinical data recorded as part of standard practice in the medical records will be entered into REDCap (secure, password protected web-based database) by local clinical and research staff. As these data will be linked with HES data at 12 months, three patient identifiers will need to be recorded. The visibility of the patient identifiers will be limited in the REDCap database. Individual consent of patient participants will not be obtained as this is not possible where data is collected retrospectively.
This approach has been comprehensively reviewed by:
-the POPS-SUp PPIE group. This comprehensive review was undertaken in the development and pilot phases of the POPS-SUp study and has been continued as the protocol has been refined
-the process of extensive peer review through the NIHR panel in order to secure the funding for POPS-SUp.

As we will be processing identifiable patient data without consent we will submit to the confidentiality advisory group (CAG) for section 251 approval.

Note that written consent is being sought from patient participants, carer/family member participants and staff participants to collect data which is not part of routine care.

8.3 National Data opt-out

The research team will check whether any patients have opted-out of their data being used for secondary purposes (such as research and planning) before including it POPS-SUp. We will use the national Data Opt-Out page and guidance to do this.

8.4 Schedule of assessments for each visit

The schedule of assessments for POPS-SUp applies to the participating hospitals as opposed to patients. NHS Elect will support the delivery of this implementation strategy through structured,

online meetings between the participating hospital site team and expert coaches (with expertise in clinical POPS services, improvement science and data management). The NHS Elect POPS programme will include:
- an initial site visit
- two-weekly team meetings
- monthly events for the cohort
- regular webinars which can be attended or viewed later according to availability.
(figure 1)

A chronological summary of study procedures is provided in table 1. This also provides an overview of the schedule of assessments.

Ethnographic observations
These observations will be undertaken by members of the research team from UCL and UoB with verbal consent having ensured that both staff and patient/ carer, family members are made aware through leaflets/posters. Observations will be undertaken of clinical interactions, local meetings and NHS Elect meetings. 150 hours in total across sites

Interviews
Some staff, patients, carers and family members will have been consented for interviews. Interviews for all of these groups will be conducted as described in this section.

Once consented the participants will be contacted by the process evaluation researchers (UCL and UoB) to arrange a suitable time and method for the interview. Participant will have the choice to be interviewed in person, by telephone or over teleconferencing software (MS Teams). The interview is unlikely to require additional visits to hospital for patients/carers/family members but if it does the costs of travel will be covered for this.

Interviews will be semi structured and expected to last 30 minutes.

Questionnaires
Patients and carers/family members will complete three questionnaires: Shared Decision Making Q9, Decisional Regret Scale and EQ-5D-5L. This part of the study will be conducted by either local clinicians or research teams or researchers from the central POPS-SUp team (GSTT, UCL, UoB).

Diary cards
These will be completed by the PI weekly directly into REDCap.

Schedule of assessment for NHS staff (conducted by the research team based at UCL and UoB)
Ethnographic observation will be conducted by the research team
Semi structured interviews will be conducted by the research team, recorded on MS Teams or digital recorders, transcribed by a transcription company. This will occur in the preimplementation phase (1st 3 months), implementation phase (6 months) and postimplementation phase (last 3 months). Interviews will occur at the staff members place of work or over teams or the phone depending on staff preference.

Schedule of assessment for patients (ethnographic observations and interviews will be conducted by the research team based at UCL and UoB)
Ethnographic observation will be conducted by the research team
Semi structured interviews will be conducted by the research team, recorded on MS teams or digital recorders, transcribed by a transcription company (see topic guide). This will occur in the

preimplementation phase (1st 3 months), implementation phase (6 months) and postimplementation phase (last 3 months).
Interviews will occur at the hospital either in the outpatient clinic or on the ward

Schedule of assessment for carers/family members
Ethnographic observation will be conducted by the research team
Semi structured interviews will be conducted by the research team, recorded, transcribed by a transcription company (see topic guide). This will occur in the preimplementation phase (1st 3 months), implementation phase (6 months) and postimplementation phase (last 3 months).
Interviews will occur at the hospital either in the outpatient clinic or on the ward

Patient/carer/family or staff participants will not need to attend additional assessment visits as part of POPS-SUp.

Once participants have completed the activities they consented to there is no further involvement from them as different people will be approached pre intra and post- implementation.

8.5 Follow up Procedures

There is no follow up procedure for patients, carers or staff in POPS-SUp.

9. END OF STUDY DEFINITION

Once HES linkage has occurred and data analysis is complete the REC/R&D will be informed that the study has been completed.

10. ASSESSMENT OF SAFETY

There are no safety concerns in the POPS-SUp study. There will be no change to the usual NHS mechanisms for reporting complaints or concerns.

10.1 Ethics Safety Reporting

There are no risks to participants in taking part in the study.

There is some risk to staff recruited by more senior staff (that they could be dependent upon for career progression), and additionally some patients recruited by clinical staff that would be dependent on their care. These scenarios raise the prospect of some power imbalances. This will be mitigated by the use of a researcher external to the clinical team conducting the qualitative interviews thus allowing staff and patients to voice accurate opinions.

10.2 Study Steering Committee

The study will be managed by the CI (GSTT), the Birmingham Centre for Observational and Prospective Studies (BiCOPS), part of the Birmingham CTU, with a dedicated costed trial manager. Regular Study Management Group (TMG) and Study Steering Committees (TSC) meetings are planned. These will be co-ordinated by BiCOPS, the CI and the trial manager.

10.3 Study Management Group

The SMG will meet monthly to oversee and manage the day to delivery of the study. The SSC will meet at least annually with an independent chair, a clinician, statistician and lay member present to advise and steer the TMG.

10.4 Ethics & Regulatory Approvals

The study requires regulatory approval form the following bodies; NHS REC favourable opinion, CAG opinion and HRA Approval. Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that the appropriate regulatory approvals have been issued, and NHS Confirmations of Capacity and Capability and Sponsor green lights are in place.

For any amendments to the study, the Chief Investigator or designee, in agreement with the Sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments as well as the study delivery team) to confirm ongoing Capacity and Capability for the study.

All correspondence with the Sponsor, REC and HRA will be retained. The Chief Investigator will notify the Sponsor and REC of the end of the study.

10.5 Ethical Considerations

This research is anticipated to be of low risk to participants. The main risks and how the team will manage them are outlined below.
POPS-SUp will be reviewed through CAG as routinely collected clinical metrics will be recorded without individual participant consent being taken. This approach has been taken due to:
-the need to minimise burden on patients and staff as stipulated by the extensive PPIE work undertaken in preparation and design of POPS-SUp
- the process of extensive peer review through the NIHR panel in order to secure the funding for POPS-SUp
- efficient and cost-effective delivery of POPS-SUp

Staff interviews: Some staff may find discussing aspects of services sensitive or stressful. To address these concerns and ensure that questions within the topic guides are sensitively presented, the team will seek feedback on the interview topic guides from the research team and PPIE partners. The team will pilot the interview topic guides to ensure that the wording of questions is appropriate. The information sheets state that participation is voluntary and that participants are free to withdraw.
Patient interviews: Some patients may find discussing aspects of services sensitive or stressful. To address these concerns and ensure that questions within the topic guides are sensitively presented, the team will seek feedback on the interview topic guides from the research team and PPI partners. The team will pilot the interview topic guides to ensure that the wording of questions is appropriate. The information sheets state that participation is voluntary and that participants are free to withdraw. We will also be able to refer patients to PALS if they require additional support.
Interviewees may be hesitant to raise criticism. To address this, the participant information sheets will highlight that researchers are independent of those delivering care and that there are no right or wrong answers. The PIS highlights that information will be fully anonymised (including names and places) and will emphasise that the researchers want to learn about things that do not work well so that they can be improved in future.
Observations: It is possible that participants taking part in the observations could feel uncomfortable having an observer watch aspects of their work. However, the PIS emphasises that the researchers

are independent of services and will abide by professional codes. In addition, the PIS makes clear that participants are free to withdraw (or ask the researcher to withdraw, if appropriate) at any time.
Loss of anonymity in data: Another risk inherent to any study involving collection of qualitative data relates to the loss of anonymity e.g. in terms of a data breach or the linking of an individuals' statements to the individual who made these statements. The secure handling and management of data is a priority of this study, and processes mitigating the associated risks are in place. In addition, recruitment documentation notes that the team cannot completely guarantee that an individual could not work out participant identity, and the option for participants not to be quoted in reports is provided.
Lone working: Interviews and professional observations may require researchers to conduct lone working. To mitigate risks associated with lone working, we have the following processes in place. Most of the interviews will take place online or over the telephone, unless there are circumstances in which interviewees prefer a face-to-face interview or find telephone or online methods inaccessible. If data collection takes place in person (COVID guidelines permitting), we will follow GSTT lone working policy and will ensure that another researcher within the team knows where the researcher is at all times and that the researcher conducting any face-to-face interviews or in-person observations checks in with the other researcher when they arrive at the destination and when they leave the destination. If the researcher feels unsafe at any time, they will leave the location immediately.

11. COMPLIANCE AND WITHDRAWAL

11.1 Participant compliance

In POPS-SUp this refers to participation at hospital site as opposed to individual patient or staff level. This means that the local PI will need to comply with POPS-SUp for 12 months. The implementation strategy has been designed to support the local PI and minimise site drop out through information gained from the two cohorts who have already participated in the POPS NHS Elect pilot. Furthermore, the implementation strategy involves monthly events and a helpline for participating sites to promote stakeholder buy-in, support with expert mentoring to minimise drop out and/or disengagement. This approach addresses the issue of insufficient engagement of professionals cited in other work (e.g. EPOCH study) as a reason for unsuccessful implementation. EPOCH also cited a lack of organisational resource and recognition of necessary time as barriers to implementing a new service. POPS-SUp pilot work showed that executive sponsor buy-in at site level and provision of a toolkit to maximise efficiency and reduce duplication of work, can address these challenges and therefore executive sponsor buy-in is required in POPS-SUp to ensure participant compliance throughout the study.

NHS staff and patient/carer/family member participant non-compliance is unlikely as there will be no follow up procedures for these individuals.

11.2 Withdrawal / dropout of participants

As POPS-SUp is testing a 'way of working' or a 'healthcare approach' and not a specific treatment it is very unlikely that the trial should need to be stopped prematurely. However, the literature will be regularly monitored and the study steering committee consulted regularly to ensure adequate management and monitoring of the study.

It is unlikely that consented participants will request withdrawal from the study due to the short time period from consent to data collection. If a consented patient wishes to withdraw from the study their views on withdrawal of their data will be sought.

It is unlikely that participants will lose the ability to consent during the study because the component where participant level consent is sought is for completion of questionnaires and a short interview and this is collected promptly after consent is given therefore making a loss of capacity in this short timeframe unexpected.

If a participant asks to opt out, following seeing a poster, they will not be included in the study. Any data already collected for the patient will be removed from the eCRF and destroyed securely.

11.3 Protocol Compliance

The CI will monitor protocol deviations and list them in a deviation log /include a file note in the TMF/Site file where applicable. The CI and sponsor must be notified immediately of a serious breach. The Breach must be reported to the REC Committee with the Sponsor in copy within 7 calendar days of the breach being confirmed as serious.

The main theoretical issue with protocol compliance in POPS-SUp is failure of adequate data collection. This potential risk has been mitigated through thorough pilot work to ensure that outcome measures are easily obtainable with the provision of NHS elect support through the POPS programme and through research infrastructure including CRN research nurses.

POPS-SUp has been designed with mitigation of the potential for incomplete data collection inherent in its design. Specifically;

- Data is collected at hospital level and not at individual patient level
- The timing of data collection is undertaken in 'real time' as part of development and implementation of the POPS service.
- Data is collected by the participating NHS staff members supported through the NHS Elect POPS programme and with specific research support from CRN research nurses
- Pilot work at other NHS sites in preparation for the POPS-SUp study demonstrated feasibility of this level of data collection

12. DATA HANDLING AND RECORD KEEPING

12.1 Source data

Source data is defined as all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical study necessary for the reconstruction and evaluation of the study.

Source data within the study will be kept as part of the participants' medical notes generated and maintained at site.

Where data is collected via patient-reported questionnaires; these are either via validated QoL measures or through additional patient reported outcomes. This data is collected on paper or electronically and inputted directly into the REDCap database system. The data inputted onto the REDCap database forms the source data. The paper questionnaires where completed form the source data in those instances.

Case Report Form Completion

An electronic case report form (eCRF) should be completed for each individual participant, and these will be electronic with the exception of the participant completed questionnaires.

If data has not been provided within four weeks of the submission schedule a reminder email will be sent to sites. If data is consistently not provided, the Trial Office will directly contact the site to ascertain the reason for the delay. This may also be escalated to the site's senior management and can trigger a monitoring visit.

In all cases it remains the responsibility of the PI to ensure that the eCRF has been completed correctly and that the data is accurate. This will be evidenced by the electronic signature of the PI or delegate(s)The **Signature & Delegation Log** will identify all those personnel with responsibilities for data collection. The delegated staff completing the CRF should ensure the accuracy, completeness and timeliness of the data reported. This will be evidenced by signing and dating the eCRF.

Data reported on eCRFs will be consistent with the source data and any discrepancies will be explained. All missing and ambiguous data will be queried. Staff delegated to complete eCRFs will be trained to adhere to trial specific working instructions on CRF Completion.

The following guidance applies to data:

- Rounding conventions - rounding should be to the nearest whole number: If the number you are rounding is followed by 5, 6, 7, 8, or 9, round the number up. (e.g. 3.8 rounded to the nearest whole number is 4). If the number you are rounding is followed by 1, 2, 3 or 4, round the number down. (e.g. 3.4 rounded to the nearest whole number is 3).
- Trial-specific interpretation of data fields – where guidance is needed additional information will be supplied.
- Entry requirements for concomitant medications (generic or brand names) – generic names should be used where possible.
- Repeat tests – the data used to inform clinical decisions should always be supplied. If a test is repeated it is either to confirm or clarify a previous reading. Confirmatory tests should use the original test values.
- Protocol and Good Clinical Practice (GCP) non-compliances should be reported to the Trial Office when become aware.

All tools that will be used are standardised validated tools.

Outcomes	Data	Timing of collection	Who will collect	Consent
Primary implementation	Reach	Weekly	Local clinical and research team	No
Primary clinical	Length of stay	Weekly	Local clinical and research team	No
Secondary implementation	Fidelity to clinical components of	Collected once in month 3 (preimplementation phase), once in	Research team	Yes (written consent from staff members)

	perioperative CGA	month 9 (implementation phase) and once in month 12 (postimplementation phase)		
	Fidelity to core components of POPS services	Collected once in month 3 (preimplementation phase), once in month 9 (implementation phase) and once in month 12 (postimplementation phase)	Research team	Yes (written consent from staff members)
	Acceptability	Collected once in month 3 (preimplementation phase), once in month 9 (implementation phase) and once in month 12 (postimplementation phase)	Research team	Yes (written consent from staff members)
	Feasibility	Collected once in month 3 (preimplementation phase), once in month 9 (implementation phase) and once in month 12 (postimplementation phase)	Research team	Yes (written consent from staff members)
Secondary clinical	Age	Once	Local clinical and research team	No
	Gender	Once	Local clinical and research team	No
	Clinical frailty scale	Once	Local clinical and research team	No
	Number of regular medications	Once	Local clinical and research team	No
	Count of comorbidities	Once	Local clinical and research teams	No
	30 day readmission	Weekly	Local clinical and research team	No
	Postoperative delirium	Weekly	Local clinical and research team	No

	Acute coronary syndrome, MI	Weekly	Local clinical and research team	No
	Cardiac failure	Weekly	Local clinical and research team	No
	Arrythmia	Weekly	Local clinical and research team	No
	Pneumonia	Weekly	Local clinical and research team	No
	Acute kidney injury	Weekly	Local clinical and research team	No
	Wound infection	Weekly	Local clinical and research team	No
	Urinary tract infection	Weekly	Local clinical and research team	No
	Catheter issue	Weekly	Local clinical and research team	No
	Fall	Weekly	Local clinical and research team	No
	Other	Weekly	Local clinical and research team	No
	Same day cancellation	Weekly	Local clinical and research team	No
	Return to preoperative place of residence	Weekly	Local clinical and research team	No
	Operative or non-operative management	Weekly	Local clinical and research team	No
	Was the initially suggested procedure undertaken or did the patient undergo a different or no procedure?	Weekly	Local clinical and research team	No
	Clinician defined, 'medically fit for discharge'	Weekly	Local clinical and research team	No
	Health economic metrics for opportunity cost Investigations Referrals to other teams Level 2/3 care.	Collected once at end of month 3 (preimplementation phase), once at end of month 9 (implementation phase) and once at end of month 12 (postimplementation phase)	Local clinical and research team	No

	Days alive and out of hospital 90 days	12 months	Research team	No
	90 day and 12 month mortality	12 months	Research team	No
	EQ-5D-5L*	Pre, during and post implementation	Research team	Yes
	SDM Q9*	Pre, during and post implementation	Research team	Yes
	DRS*	Pre, during and post implementation	Research team	Yes

*

- HRQoL(EQ-5D-5L) (collected in a consented subgroup of patients) to be collected in the preimplementation and in postimplementation phase
-Shared decision making (SDMQ9) (collected in a purposively sampled consented subgroup of patients) to be collected in the preimplementation and in postimplementation phase
-Decisional regret (Decision Regret Scale) (collected in a purposively sampled consented subgroup of patients) to be collected in the preimplementation and in postimplementation phase
(6 patients per site to be consented in each of the pre and post implementation phases across 18 sites. Purposive sampling to include elective/emergency, surgery/no surgery and LoS</> 5 days. Applies to SDMQ9 and DRS. Estimated total 216 patients)

Table 2 – details of data collection

Data collection for the process evaluation
Data collection will include:
Semi structured interviews (audio recorded on MS teams or using digital recorders)
Documentation of how rollout strategies are implemented in practice, factors that might be acting as barriers and enablers in the rollout and aspects of the intervention and rollout that need improvement (notes)
Documentary analysis related to the implementation of the intervention (i.e., business case, action-effect diagrams and preferred outcome measures) (notes)
Ethnographic observations (notes)

Data analysis for the process evaluation
The evaluation will use a formative design where findings are shared with the implementation team on a regular basis to inform implementation. Rapid analysis techniques (where data are analysed in parallel to data collection) and feedback loops will be used to facilitate the sharing of emerging findings. Framework analysis (Gale et al. 2013) will be used to carry out more in-depth analysis, bringing together the interview, observational and documentary data to create individual case studies and explore variation in implementation. The framework will be informed by the CFIR, but we will also be sensitive to new topics emerging from the data.

Health economic analysis
Our primary analysis will be an incremental cost-consequences analysis (CCA) of the implementation and delivery of POPS at scale with pre-implementation care and its associated outcomes providing the study comparator. We will estimate the incremental cost of health care resource inputs utilised in both the implementation strategy for scaling up POPS services across all 18 sites and in its on-going delivery as a perioperative model of care in routine clinical practice (compared against perioperative care costs in the absence of POPS). Incremental costs will be presented alongside evidence of the incremental effect of POPS services across multiple outcome domains, including

implementation outcomes, clinical outcomes, and patient focussed outcomes (e.g. acceptability, and quality-of-life). Patient level data on resource utilisation provided through local data management systems will be used to implement a decision analytic model focussed on quantifying the cost consequences of implementing POPS, including resource impacts mediated through any reduction in postoperative complications. A secondary cost-utility analysis (CUA) will be undertaken that will use quality of life data collected locally through this study and drawing on long-term QALY modelling from an existing published study. The CUA will be used to estimate the incremental cost per quality-adjusted life year gained associated with wider adoption of POPS across the study sites and how this compares to current cost-effectiveness thresholds used in NHS resource allocation guidance.
All economic analyses will be undertaken through a combination of statistical analysis of site- and patient-level cost data (informed by the main study statistical design outlined in the SAP) and using decision analytic modelling.

12.2 Data Management

Processes will be employed to facilitate the accuracy and completeness of the data included in the final report. These processes will be detailed in the trial specific Data Management Plan (DMP) and include the processes of data entry and data queries.

Data entry will be completed by sites via a BICOPS managed trial database, however, questionnaires returned to the Trial Office will be entered by a member of the trial team at the Trial Office via the same trial database. The data capture system will conduct automatic range checks for specific data values to ensure high levels of data quality. Queries will be raised using data clarification forms (DCFs) via the trial database, with the expectation that these queries will be completed by the site (ideally) within 30 days of receipt. Overdue data entry and data queries will be requested on a regular basis.

Self-evident corrections will be only be permitted when entering participant completed questionnaires to correct date fields, or complete logic trees to allow entry of participant reported data, within the returned forms, by the Trial Office.

Data Security

UoB has policies in place, which are designed to protect the security, accuracy, integrity and confidentiality of Personal Data. The study will be registered with the Data Protection Officer at UoB and will hold data in accordance with the Data Protection Act (2018 and subsequent amendments). The CHAPTER Study Office has arrangements in place for the secure storage and processing of the study data which comply with UoB policies.

The Study Database System incorporates the following security countermeasures:

Physical security measures: restricted access to the building, supervised onsite repairs and storages of back-up tapes/disks are stored in a fire-proof safe.

Logical measures for access control and privilege management: including restricted accessibility, access controlled servers, separate controls of non-identifiable data.

Network security measures: including site firewalls, antivirus software and separate secure network protected hosting.

System management: the system will be developed by the BiCOPS Team at the CHAPTER Study Office, and will be implemented and maintained by the BiCOPS Team.

System design: the system will comprise of a database and a data entry application with firewalls, restricted access, encryption and role-based security controls.

Operational processes: the data will be processed and stored within BiCOPS.

Data Protection Registration: UoB's Data Protection Registration number is Z6195856.

Prior to HES linkage data will not be pseudonymised. However it will be kept in a secure password protected database (REDCap). Identifiers being collected for HES linkage are being entered into a separate but linked page of the REDCap database which is permission accessed. All other data entered into the database will be pseudonymised.
Figure 4 data flow diagram

Process evaluation
University College London are conducting this aspect of the study on behalf of the Sponsor.

The study is compliant with the requirements of General Data Protection Regulation (2016/679) and the Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing and disclosure of personal information, and will uphold the Act's core principles.

Audio recordings and written material will be collected from participants in accordance with the PIS, consent forms and the processes outlined in this protocol. Interviewees will be consented for electronic audio recording on a portable encrypted voice recorder belonging to the research group. Audio recordings might also be made on platforms such as MS Teams. These recordings will be securely stored by the researcher on the UCL server before being appropriately sent for professional transcription to TP transcription(http://tptranscription.co.uk/). Automatic transcripts might also be generated using the MS teams transcript option. Transcripts will be anonymised upon their receipt or when generated via MS Teams. Field notes from meeting observations and documentary analysis will be anonymised as they are written up into electronic format.

Participants will be assigned anonymous identifier codes rather than recording their names. These codes, and a description of participants' roles, will be stored in a password-protected file on a secure drive to which only the core research team has access. The only personal data we will collect will be their contact details including full names, telephone numbers and e-mails for those who would like to be interviewed over the telephone or virtual video software programme. Personal data will be recorded in a secure server at UCL. After the interview, the contact details will be deleted.

Audio recordings and electronic data relating to the study (including interview transcripts) will be stored in a secure server at UCL. Access to data is granted after login with valid accounts and according to access permissions. All paper documentation relating to the study will stored securely with restricted access within UCL. The data can only be accessed by identified UCL researchers. This data will not be transferred to any party not identified in the study protocol and are not to be processed and/or transferred other than in accordance with the participants' consent. The research team will process, store and dispose of audio and written participant data in accordance with Sponsor

instruction and all applicable legal and regulatory requirements, including the Data Protection Act 1998 and any amendments thereto.

All data will be stored for 5 years after study completion.
After study closure, each collaborating organisation and participating site will archive their research data in accordance with instructions from the sponsor. The process of destroying documents will be in accordance with standard procedures of the sponsor.

12.3 Data sharing

Requests for data generated during this study will be considered by the POPS-SUp study team. Data will typically be available six months after the primary publication.

Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BiCOPS Data Sharing Committee in discussion with the CI and, where appropriate (or in absence of the CI) any of the following: the Study Sponsor, the SMG, and the SSC.

A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers transfer of participant identifiable information.

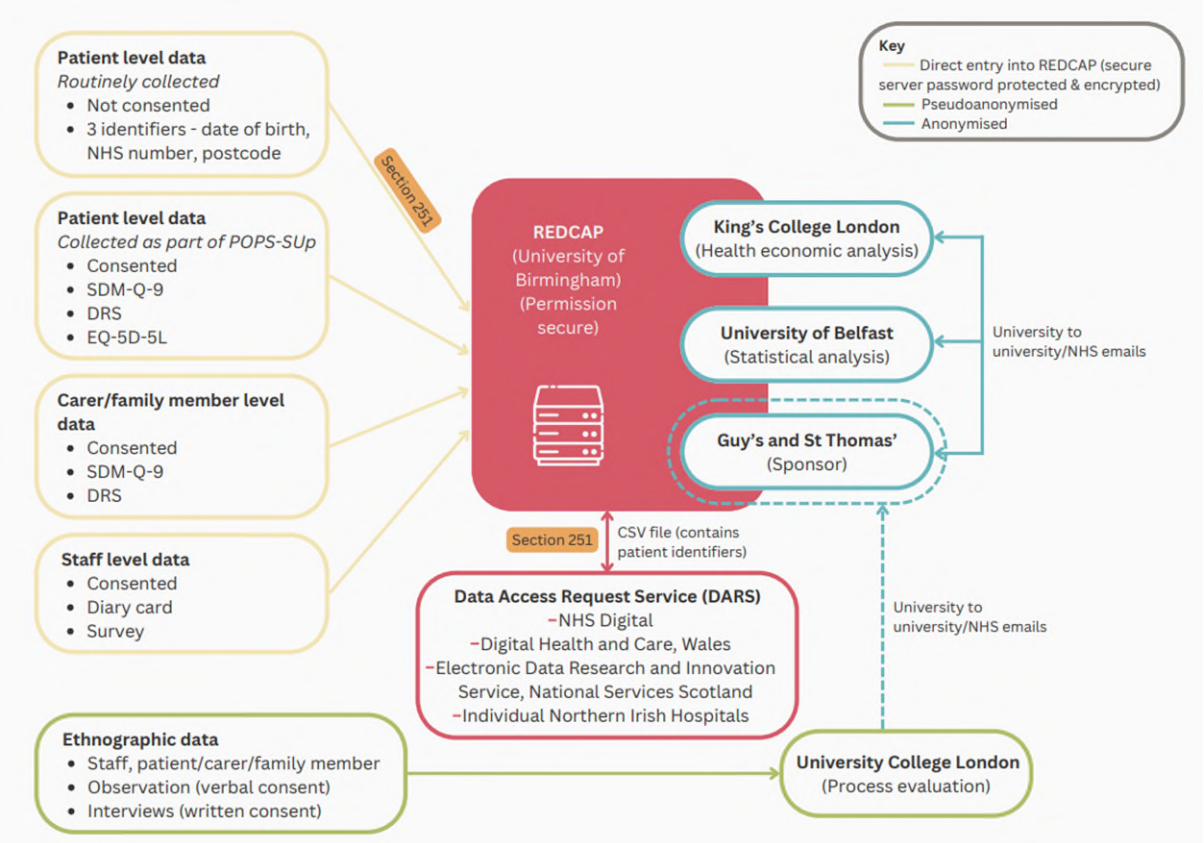

Figure 4 Data flow diagram

Process evaluation
Audio recordings from the interviews will be securely stored by the researcher before being appropriately sent for professional transcription to TP transcription(http://tptranscription.co.uk/).

Transcripts will be anonymised upon their receipt. The UCL research team and TP transcription have a data sharing agreement in place. Audio recordings sent from the team to TP transcription and the returned transcripts are shared via a secure online portal managed by TP transcription.

12.4 Personal Data Breaches

GDPR broadly defines personal data breaches as a security incident that has affected the confidentiality, integrity or availability of personal data. In short, there will be a personal data breach whenever any personal data is lost, destroyed, corrupted or disclosed; if someone accesses the data or passes it on without proper authorisation; or if the data is made unavailable, for example, when it has been encrypted by ransomware, or accidentally lost or destroyed.

Personal data breaches will be immediately reported to the Sponsor/data controllers and to the Data Protection Officer/IG Department of the site that incurred the breach. The following information will be provided to assess the full risk/impact of the breach: full details as to the nature of the breach, an indication as to the volume of material involved, and the sensitivity of the breach (and any timeframes that apply), steps that have been taken to mitigate the risk (trying to retrieve the data asking third parties to delete information that was sent to them in error).

Sites will additionally follow their Trust incident reporting mechanisms and will document this within their TMF/ISFs in the form of a file note provided by the sponsor with corrective and preventative measures addressed.

The sponsor/data controller will determine whether the breach meets the definition of a serious breach and warrants reporting to the regulators including the ICO https://ico.org.uk/for-organisations/report-a-breach/personal-data-breach-assessment/

13. MONITORING AND AUDITING

The Chief Investigator will be responsible for the overall ongoing management of the study but may delegate specific activities to collaborating organisations where this is covered by an appropriate agreement/contract. The Sponsor will monitor and conduct audits on a selection of studies in its clinical research portfolio. Monitoring and auditing will be conducted in accordance with the UK Policy Framework for Health and Social Care and in accordance with the Sponsor's monitoring and audit procedures.

14. STATISTICAL CONSIDERATIONS

Sample size

An unweighted one sample t-test with each of 18 sites contributing a single after-before data point would have 90% power at 5% level of significance to detect an effect size of 0.8 i.e., a difference in mean length of stay after over before implementation of 0.8 standard deviations. If the standard deviation at the site level was five days, this would equate to being able to detect a mean difference of four days, which would be sufficient to impact clinical practice.

The true power of the study will be greater (for example, allowing us to detect a smaller mean difference, of two-three days) and will be accurately assessed using simulation informed by early data from the study, and using the statistical model to be employed, which will depend on individual level data within each site, potentially at multiple time points (e.g. each week for around 12 times in each of the three month before and after periods), and fully account for dependency across participants within sites, and adjusting for known prognostic factors.

At present, we are expecting each site to contribute on average 15 participants per month, with NELA data showing a median length of stay of ten days in those without return to theatre.

Statistical Analyses Plan

General: The analysis of the interrupted time series will adopt the recommendations of Cruz 2017 (in particular providing flexibility to model evolving variability and correlation between the before and after periods) and follow the useful guidance of Bernal 2018.

Rationale for ITS design: The randomised controlled trial (RCT) is seen as the gold standard design, allowing causal interpretation of the estimated intervention effect. The RCT design relies on being able to randomise individuals or groups of individuals (clusters) to intervention or control. Given the current status of CGA deployment in the NHS, such randomisation would not be feasible across clinicians and participants.

We did consider a stepped wedge design, often seen as useful when evaluating the performance of an intervention which is going to be implemented. However, there are substantial logistical challenges that made such a stepped wedge design not likely workable.

Instead, we chose the Interrupted Time Series (ITS) design that would allow evaluation of CGA by comparing the level and trend of carefully specified outcome after the intervention compared with that before the intervention. We did also consider a Differences-in-Differences design but felt the ITS design is particularly suited to interventions introduced at a population level over a clearly defined time period that target population level outcomes (Bernal 2017).

In addition, the ITS design here uses routine recorded data (primary outcome length of hospital stay, with data aggregated at the site level) on a largely unselected cohort (there is no consent process, and the intervention will be delivered by existing staff doing their usual jobs) and hence external generalisability should be strong [53, 54].

See also 39, 55, 56, 57, 58 for additional details on various design considerations for the ITS. See 59 for an instructive example of the reporting of an ITS designed study.

Analysis population. The primary analysis will include all participants recruited in the study where possible (akin to an 'intention to treat' analysis, consistent with a treatment policy estimate and (ICH E9(R1) – see 60, 61).
Trial Periods: There will be 2 periods, each of 12 months, each recruiting from 9 sites (no site in the first period will contribute to the second period).

Time Structure: The intended structure of each period will be 3:6:3 months of Before: Implementation: After, and the intention of the analysis will be to estimate the effect of the intervention by comparing the After – Before.

Compliance/Fidelity: This is a statistical analysis plan for the effectiveness part of a hybrid implementation-effectiveness study. Compliance with the intervention and/or fidelity of the implementation of the intervention is being measured and assessed separately in the POPS-sUP process evaluation. There will not be any statistical modelling (e.g., causal effect modelling) to adjust the treatment effects for any measure of compliance.

Statistical Reporting. In general terms, categorical data will be presented using counts and percentages, whilst continuous variables will be presented using the mean, median, standard

deviation (SD), minimum, maximum, Q1, Q3, inter-quartile range (IQR) and number of patients with an observation (n).

Graphical analysis. We will produce boxplots, i.e., a graphical summary of the distribution including mean, median, first and third quartile, minimum and maximum values, for before and after the intervention, and by site, and period.

Recruitment rate: The expected recruitment rate is average 15 recruits per month per site. So, a site will be expected to contribute 180 patients over 12 months; and over a period (12 months) the 9 sites are expected to contribute 1620 patients; and over the 2 periods (the total for the study) will be expected to be 3240 patients.

Follow up: The length of stay of all those recruited will be followed up, including follow up occurring outside the recruitment month.

Primary Outcome: The primary outcome (for clinical effectiveness) is length of hospital stay.

Measurement: This will be measured on an individual basis as the total length of hospital stay, including any re-admission within 30 days of discharge.

Shape of treatment response. Following Cruz (2017) [41] we will estimate the shape of the treatment response from the data, but also from Bernal (2018) [62,63] we anticipate that the shape of the treatment response will incorporate (a) a gradual change in the slope (trend) and (b) a gradual change in the 'step' (intercept) and (c) it is a possible there may be a delay (lag) in either or both of these effects (slope and intercept).

Statistical model. A times series model with a continuous outcome (on either length of stay or log10(length of stay) to address skewness, with estimates and 95% confidence intervals back-transformed to the original untransformed scale, days) [64,65].

Model terms: We will estimate the effect of the intervention on the co-primary outcome of (untransformed or transformed) length of hospital stay, with terms for treatment (after – before periods, within site) accounting for any deaths, and adjusting for local site effects (including staggered times of intervention) and any temporal trends (potentially non-linear), and adjust for either site or individual level covariates strongly related to the outcome.

Periods: We will adjust for the two cohorts (first cohort n=9 sites, first period of 12 months; and second cohort n=9 sites, second period of 12 months; a total of 18 sites over a two 12-month periods).

Model assumptions: All the assumptions regarding the statistical model will be assessed, including (a) autocorrelation structure, and (b) non-stationarity and (c) seasonality, if appropriate.

Units of measurement and analysis: The length of stay will be measured at the individual level and analysed at the site level, in a time unit of one week (to be confirmed at the sample size re-estimation step at the end of the first period) i.e., all those recruited in a site in a specific week, meaning that the expectation is that a site will contribute 13 before and 13 after data points, each aggregating on average 3-4 patients.

Secondary Outcomes: The secondary outcomes (e.g., 30-day re-admission, Comprehensive Complications Index, return to pre-op residence, days alive out of hospital at 90 days, mortality at 90 days and 1 year, and the quality of life measures) will be analysed in a similar way to the primary outcome with a statistical model appropriate for the specific secondary outcome (e.g. binary or ordinal logistic regression, time-to-event (Cox) regression, linear regression).

Subgroup Analyses: Pre-defined Subgroup analysis will be restricted to the primary clinical effectiveness outcome alone. Any further subgroup analysis (e.g., if suggested later by new data external to the study) will be labelled exploratory. Pre-specified subgroup analyses will be unlikely to be adequately powered.

Missing data: We do not anticipate much missing data on the primary outcome (length of stay). Nonetheless, we will check the robustness of the findings to any patterns of missing data using sensitivity analyses (including multiple imputation under an assumption of missing at random, or possibly pattern mixture type models for informative missingness) [66].

A multiple imputation approach will be used assuming the data are missing at random. In addition, and probably more consistent with the likely missing data generating mechanisms, sensitivity type analyses assuming the data are missing not at random (i.e., informatively missing) will be explored e.g., using pattern mixture models, or tipping-point type approaches.

These sensitivity analyses would attempt to identify different types of missing data by an underlying reason or reasons, and then imputing values that capture plausible measurements for those missing data.

The (gamma) γ-adjustment approach [67] will be followed, and also the recommendations on sensitivity analyses [68].

Safety: The safety data (e.g., medical and surgical complications, factors around delayed discharge, delirium, acute coronary syndrome, cardiac failure, arrythmias, pneumonia, wound infection, urinary tract infections, faecal incontinence, falls, acute post-op complications (cardiac, pulmonary, infections, bowel/bladder, vascular), level 2/3 care post-surgery; and other adverse events) will be presented descriptively.

Interim and Final Analysis: This analysis plan describes the end of trial statistical analyses to be performed for POPS-sUP.

There will be no formal interim analyses.

There will be a sample size check / re-estimation step at or around the end of the first cohort of 9 sites followed for the first 12 months, which will validate the assumptions behind the power calculation (specifically the assumed common standard deviation) and in particular upgrade the estimation of the actual power of the study using simulation, using the appropriate statistical model for the primary outcome of length of stay, instead of the simple approximation using a 1-sample t-test as above. The timing of the sample size re-estimation coincides with the end of the first period of 12 months. See 69 and 40 for further details on sample size estimation in ITS designs.

Control series. Although including a control condition can be useful in the estimation and interpretation of the modelled primary outcome, there was no obvious candidate outcome here and for simplicity this option was not pursued (see 62,63 for further details).

Tables and Figures: for the Statistical Report – to be specified.

Statistical software: All analysis and data manipulation will be carried out using SAS or R for Windows or Stata unless otherwise stated [70,71,72].

Data sharing: A file, or set of files, containing the final data will be prepared, along with a data dictionary. These will be made available to the Chief Investigator at the end of the analysis phase.

15. PEER REVIEW

POPS-SUp has been extensively peer reviewed through various processes;
Competitive NIHR HS&DR funding call
Competitive award of THIS Institute Fellowship to develop the POPS-SUp study
Award of SEL cancer money to develop POPS-SUp
Presentation through King's College London – GSTT research meeting for critical appraisal
PPIE 1 – patient and carer review
PPIE 2 – community of practice (NHS elect pilot sites)
PPIE 3 – professional stakeholders

16. FINANCING

Funding call: 22/135 NIHR James Lind Alliance Priority Setting Partnerships rolling call (HSDR Oct 2022 - Jan 2023). 157443
Amount awarded: £1,540,771.70
Start date: 1.2.24
Duration: 39 months

17. INSURANCE AND INDEMNITY

This study is sponsored by Guy's and St Thomas' NHS Foundation Trust (GSTFT) and indemnity is provided through NHS Resolution's Clinical Negligence Scheme for Trusts (CNST) which provides indemnity for clinical negligence. In the case of negligent harm, health care professionals undertaking clinical trials or studies on volunteers, whether healthy or patients, in the course of their NHS employment are covered by NHS Resolution. In the case of non-negligent harm, legal liability does not arise where a person is harmed but no one has acted negligently. In exceptional circumstances NHS bodies may consider whether an ex-gratia payment could be offered.

18. DATA CONTROLLER

Guy's and St Thomas' NHS Foundation Trust is the Data Controller as defined by UK general data protection legislation (UK GDPR) for this study and as such agrees to comply with the obligations placed on a Data Controller by the UK GDPR. This is not limited to, but includes, being responsible for and able to demonstrate compliance with the principles relating to Processing of Personal Data (Article 5 UK GDPR).

19. INTELLECTUAL PROPERTY

Any IP generated by the study will owned by the Sponsor and the CI, Professor Jugdeep Dhesi.

20. REPORTING AND DISSEMINATION

This will be the first trial assessing implementation and clinical and cost effectiveness of CGA-based POPS services at scale in the NHS. This will end uncertainty about how to implement CGA-based perioperative care for patients undergoing elective and/or emergency general and/or orthopaedic and/or urological and /or vascular surgery, and potentially save lives, improve quality of life, and reduce healthcare costs. This will be the main output of this research and will guide all future care in this clinical area. We envisage this work to have an impact at individual (patient and clinician), organisational and policy level. We have therefore conducted a stakeholder mapping exercise and ensured all relevant stakeholders for dissemination and maximal impact have been identified.

Intended outputs from POPS-SUp

Dissemination to key audiences (aligned with the mapping of stakeholders) will take place in lay and expert format, via:

An **annual networking event** in the form of a hybrid (online and face-to-face) workshop for both key evidence users including patient facing charities, practitioners, health service managers/decision makers and experts from all perioperative healthcare backgrounds. This will be a one day event, hosted by the British Geriatrics Society (with lay representation) led by the CI and research team supported by the NHS Elect POPS team, Birmingham CTU and with our PPI/E partners and support from the PPI co-ordinator to promote ongoing dialogue and ensure needs of evidence users remain central to research.

Nine monthly lay and expert **updates published on a study website**, and key project milestones will be shared via **social media** (X, Facebook), prepared with our PPI/E partners and research team, including infographics and videos recognising that different stakeholders access research information in different formats.

We will work closely with relevant patient organisations at all stages of the project to share our research updates and findings as we recognise that these organisations are key conduits for research dissemination to members of the public. We use a variety of media including infographics and videos as well as printed material to do so.
Conference presentations during the study, will be used to share findings with researchers and clinicians working with organisations such as the British Geriatrics Society, Evidence Based Perioperative Medicine, Centre for Perioperative Care, Association of Surgeons of Great Britain and Ireland, Vascular Society and similar international annual conferences.

Peer reviewed **publications** in medical journals (open access).

Guidelines NICE and international bodies (CI and research team members sit on several NICE and international committees).

Healthcare policy We will regularly liaise with key decision makers so that our research will shape healthcare policy. This will be facilitated by our existing relationships and networks and our co-applicants with roles at National Health Service England, Getting It Right First Time, National Emergency Laparotomy Audit, British Geriatrics Society, Centre for Perioperative Care.

Engagement of patients/service users, carers, NHS, social care organisations and the wider population about findings from POPS-SUp

Patients, carers and the wider population

Our PPI/E partners have informed the development of patient-facing study information and our proposed dissemination strategy including supporting materials. We have engaged with patient facing organisations such as Age UK, Independent Age and South Asian Health Action as well as the Patient Information Forum, to help inform and engage patients and carers and to develop materials and ensure dissemination according to patient preference. Specifically, our PPI/E partners have told us they would like to receive information through a variety of channels; in person, written and video (including use of animation if possible). We have costed accordingly for these communication platforms.

Professionals and NHS and social care organisations

We will ensure the widest possible engagement and dissemination of POPS-SUp findings to perioperative, surgical and geriatric medicine healthcare professionals and organisations. All co-applicants will exploit their networks and relationships to ensure interim and final findings are shared with individual professionals, professional organisations and decision/policy makers. Pertinently, the CI, co-applicants and collaborators have established roles at all major perioperative healthcare societies in the UK, facilitating timely dissemination to NHS healthcare professionals. In particular, the CI is the British Geriatrics Society President Elect and deputy director at the Centre for Perioperative Care. Our strategy of publishing outputs in multiple, accessible formats on a study-specific website, social media, and directly communicating these to NHS and perioperative healthcare societies, will ensure the widest possible reach during POPS-SUp and on study completion. We will ensure that the findings of the study are immediately disseminated to NICE, since representatives from the research team are members of a NICE Technology Appraisal Committee. Co-applicants will ensure dissemination to policy makers at NHSE and the Health Foundation.

<u>Ensuring outputs from POPS-SUp enter our health and care system and society as a whole?</u>

The results from this study will influence and alter clinical practice. They will enter the health and care system in the UK via influence of NICE NG180. A key research recommendation from this guideline was to appraise the clinical and cost effectiveness of preoperative optimisation, which is directly addressed by POPS-SUp. The results will be shared with NICE and healthcare professionals and commissioning groups. Fundamentally, this will lead to more effective implementation of POPS services, maximising the benefits for patients with cost effectiveness for the NHS.

We anticipate that the results will enter the wider perioperative sphere via informing guidelines published by the Centre for Perioperative Care, British Geriatrics Society, Anaesthesia Association, Royal College of Surgeons, and American Geriatrics Society, National Surgical Quality Improvement Programme (USA). The results of POPS-SUp will influence guidelines and clinical practice globally.

The implementation scientists in our research team will share the lessons learnt from the coproduced POPS-SUp implementation strategy with other health and social care sectors. Sharing of such lessons will inform cross-specialty learning about effective implementation of complex interventions.

This will ensure POPS-SUp has an impact beyond the perioperative setting, with potential benefit for other patient groups across health and social care sectors. For example, implementation and evaluation of complex interventions for children living with long term medical conditions or implementation and appraisal of multicomponent interventions to target public health challenges.

<u>Will further funding or support be required if POPS-SUp is successful (e.g. from NIHR, other Government departments, charity or industry)?</u>

POPS-SUp will demonstrate how to implement POPS services throughout the NHS with cost effectiveness. Following completion of the study, we anticipate support will be required from key organisational stakeholders. We have secured collaborator's letters from each of these organisations to disseminate findings and effect change in a timely fashion, ensuring equitable access for all patients regardless of geography, ethnicity or socioeconomic status.

21. REFERENCES

1 Fowler A, Abbott T, Prowle J et al. Age of patients undergoing surgery. Br J Surg 2019; 106: 1012–8. doi.org/10.1002/bjs.11148

2 Parmar KL, Law J, Carter B et al. Frailty in older patients undergoing emergency laparotomy: results from the UK observational emergency laparotomy and frailty (ELF) study. Ann Surg. 2021; 273(4): 709-718. doi: 10.1097/SLA.0000000000003402

3 Fowler AJ, Hussein Wahedally MA et al Death after surgery among patients with chronic disease: prospective study of routinely collected data in the English NHS. Br J Anaesth. 2022 Feb; 128(2): 333-342. doi: 10.1016/j.bja.2021.11.011

4 Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older; morbidity and mortality from major non cardiac surgery J Am Geriatr Soc 2005; 53(3):424-9 doi:10.1111/j.1532-5415.2005.53159.x.

5 https://www.bgs.org.uk/resources/resource-series/comprehensive-geriatric-assessment-toolkit-for-primarycare-practitioners

6 Ellis G, Gardner M, Tsiachristas A et al. Comprehensive geriatric assessment for older patients admitted to hospital (review). Cochrane Database Syst Rev 2017 Issue 9; CD006211. doi:10.1002/14651858.CD006211.pub3.

7 Partridge JS, Harari D, Martin FC et al. Randomized clinical trial of comprehensive geriatric assessment and optimization in vascular surgery. Br J Surg 2017; 104: 679–87. doi.org/10.1002/bjs.10459

8 Partridge JSL, Healey A, Modarai B et al. Preoperative comprehensive geriatric assessment and optimisation prior to elective arterial vascular surgery; a health economic analysis. Age and Ageing 2021; 50(5): 1770-1777.doi: 10.1093/ageing/afab094

9 Eamer G, Taheri A, Chen SS et al. Comprehensive geriatric assessment for older people admitted to a surgical service. Cochrane Database Syst Rev 2018; Issue 1: CD012485. doi:10.1002/14651858.CD012485.pub2.

10 Aitken RM, Partridge JSL, Oliver CM et al. Older patients undergoing emergency laparotomy: observations from the National Emergency Laparotomy Audit (NELA) years 1–4. Age Ageing 2020; 49: 656–63. doi.org/10.1093/ageing/afaa075

11 https://www.cpoc.org.uk/sites/cpoc/files/documents/2021-09/CPOC-BGS-Frailty-Guideline-2021.pdf

12 https://www.rcseng.ac.uk/library-and-publications/rcs-publications/docs/the-higher-risk-general-surgicalpatient/

13 https://data.nela.org.uk/reports/hospital-reports.aspx

14 Joughin A, Partridge J, O'Halloran T, Dhesi J. Where are we now in perioperative medicine? Results from a repeated UK survey of geriatric medicine delivered services for older people. Age Ageing 2019; 48: 458–

62. doi:10.1093/ageing/afy218

15 https://www.gettingitrightfirsttime.co.uk/medical-specialties/anaesthesia-perioperative-medicine/

16 https://www.health.org.uk/publications/the-spread-challenge

17 Fulop NJ, Ramsay AIG, Perry C et al. Explaining outcomes in major system change: a qualitative study of implementing centralised acute stroke services in two large metropolitan regions in England. Implementation Sci 2016;11(1):80 doi.org/10.1186/s13012-016-0445-z

18 Shahab R, Lochrie N, Moppett IK et al. A Description of Interventions Prompted by Preoperative Comprehensive Geriatric Assessment and Optimization in Older Elective Noncardiac Surgical Patients. JAMDA 2022; 23(12):1948-1954 doi.org/10.1016/j.jamda.2022.08.009

19 Siu ATY, Poulton T, Ismail, H et al. Prehabilitation in older people; Current developments. Current Anaesthesiology Reports 2021; 11: 373–380 doi.org/10.10075/s40140-021-00496-9

20 Tew GA, Caisley K, Danjoux G. Preoperative exercise training for adults undergoing elective major vascular surgery: A systematic review. Plos One. 2022;17(1):e0263090 doi:10.1371/journal.pone.0263090

21 McIsaac DI, Hladkowicz E, Bryson GL et al Home-based prehabilitation with exercise to improve postoperative recovery for older adults with frailty having cancer surgery; the PREHAB randomised clinical trail. Br J Anaesth 2022; 129(1):41-48 doi.org/10.1016/j.bja.2022.04.006

22 Dele Casas R, Meilak C, Whittle A, et al. Establishing a perioperative medicine for older people undergoing surgery service for general surgical patients at a district general hospital. Clinical Medicine 2021;21(6): e608–14 doi:10.7861/clinmed.2021-0356

23 Thillainadesan J, Aitken SJ, Monaro SR, et al. Geriatric Comanagement of Older Vascular Surgery Inpatients Reduces Hospital-Acquired Geriatric Syndromes. J Am Med Dir Assoc. 2022 Apr;23(4):589-595.e6. doi:10.1016/j.jamda.2021.09.037.

24 Jasper EV, Dhesi JK, Partridge JS, Sevdalis N. Scaling up perioperative medicine for older people undergoing surgery (POPS) services; use of a logic model approach. Clin Med (Lond). 2019; 19:478–84 doi:10.7861/clinmed.2019-0223

25 Kocman D, Regen E, Phelps K et al. Can comprehensive geriatric assessment be delivered without the need for geriatricians? A formative evaluation in two perioperative surgical settings. Age Ageing 2019; 48(5): 644-649 doi:10.1093/ageing/afz025

26 Peden CJ, Stephens T, Martin G et al. Effectiveness of a national quality improvement programme to improve survival after emergency abdominal surgery (EPOCH): a stepped-wedge cluster-randomised trial. Lancet 2019;393(10187): 2213-2221. doi:10.1016/S0140-6736(18)32521-2

27 Skivington K, Matthews L, Simpson SA et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021; 374: n2061 doi:

10.1136/bmj.n2061.

28 Moore G, Campbell M, Copeland L et al. Adapting interventions to new contexts—the ADAPT guidance. BMJ 2021; 374:n1679 doi.org/10.1136/bmj.n1679

29 Partridge JSL, Ryan J, Dhesi JK, The CPOC-BGS perioperative frailty guideline group. New guidelines for the perioperative care of people living with frailty undergoing elective and emergency surgery—a commentary. Age Ageing 2022; 51:1-12 doi.org/10.1093/ageing/afac237

30 Waring J, Martin G, Partridge JSL, Dhesi JK Implementing a Perioperative care of Older People undergoing Surgery (POPS) service: findings from a multi-site qualitative implementation study. Revision submitted to Age Ageing May 2023.

31 Lodge M, Dhesi JK, Shipway DGH, et al Factors associated with implementing the perioperative medicine for older people undergoing surgery (POPS) service. Revision submitted to Age Ageing May 2023.

32 https://cfirguide.org

33 Powell BJ, Waltz TJ, Chinman MJ et al. A refined compilation of implementation strategies: results from the Expert Recommendations for Implementing Change (ERIC) project. Implementation Sci 2015;10: 21 doi.org/10.1186/s13012-015-0209-1

34 Fowler AJ, Dobbs TD, Wan YI et al. Resource requirements for reintroducing elective surgery during the COVID-19 pandemic: modelling study. British Journal of Surgery 2021; 108 (1): 97–103 doi.org/10.1093/bjs/znaa012

35 Whitty CJM, MacEwan C, Goddard A et al. Rising to the challenge of multimorbidity. BMJ 2020;368:6964 doi.org/10.1136/bmj.l6964

36 https://www.nihr.ac.uk/about-us/our-key-priorities/equality-diversity-and-inclusion/

37 Dawson S, Banister K, Biggs K et al. Trial Forge Guidance 3: randomised trials and how to recruit and retain individuals from ethnic minority groups—practical guidance to support better practice. Trials 2022;23: 672 doi.org/10.1186/s13063-022-06553-w

38 https://www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-researchguidance-from-include-project/25435

39 Bernet AC, Willens DE, Bauer MS Effectiveness-implementation hybrid designs: implications for quality improvement science. Implementation Sci 2013;8:S2. doi.org/10.1186/1748-5908-8-S1-S2

40 Hawley S, Ali MS, Berencsi K et al. Sample size and power considerations for ordinary least squares interrupted time series analysis: a simulation study. Clin. Epidemiology 2019; 11; 197-205. doi:10.2147/CLEP.S176723

41 Cruz M, Bender M, Ombao H. A robust interrupted time series model for analysing complex healthcare intervention data. Statistics In Medicine, 2017; 36; 4660-4676 doi:10.1002/sim.7443

42 Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. Int J Epidemiology 2016; 46(1); 348-355 doi:10.1093/ije/dyw098

43 https://ilcuk.org.uk/trial-and-error/

44 Shaw RB, Sweet SN, McBride CB, et al Operationalizing the reach, effectiveness, adoption, implementation, maintenance (RE-AIM)) framework to evaluate the collective impact of autonomous community programs that promote health and well-being BMC Public Health 2019; 19803 doi.org/10.1186/s12889-019-7131-4

45 Scholl I, Kriston L, Dirmaier J, et al. Development and psychometric properties of the Shared Decision Making Questionnaire–physician version (SDM-Q-Doc) Patient Educ. Couns. 2012;88(2):284–290. doi.org/10.1016/j.pec.2012.03.005

46 Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. Med Decis Making. 2003 Jul-Aug;23(4):281-92. doi: 10.1177/0272989X03256005.

47 Drummond M, Sculpher M, Torrance G et al (2005). Methods for the Economic Evaluation of Health Care Programmes. Oxford, Oxford University. Press. https://www.rds-london.nihr.ac.uk/wpcms/wpcontent/uploads/2018/09/Cost-consequences-analysis-an-underused-method.pdf

48 https://www.nice.org.uk/process/pmg9/chapter/the-reference-case.

49 https://www.gov.uk/government/collections/nhs-reference-costs

50 https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/

51 Law KY, Cross J, Dhesi KL, Partridge JSL. Developing the workforce to deliver perioperative medicine for older people undergoing surgery – a Transdisciplinary Education Programme [under review by Future Healthcare Journal]

52 Stewart JJ, Partridge JSL, Dhesi JK. Perioperative medicine for Older People undergoing Surgery (POPS): Comprehensive Geriatric Assessment (CGA) and optimization in the perioperative setting. International Anesthesiology Clinics 2023; 61:2. doi:10.1097/AIA.0000000000000396

53 Barnighausen T, Oldenburg C et al. Quasi-experimental study designs series – paper 7: assessing the assumptions. J Clin Epidemiol 2017; 89; 53-66

54 Barnighausen T, Tugwell P et al. Quasi-experimental study design series – paper 4 uses and values. J Clin Epi 2017; 89; 21-29

55 Bhaskaran K et al. Time series regression studies in environmental epidemiology. Int J Epidemiol 2013; 42; 1187-1195

56 Zhang Y, Ren Y et al. Design and statistical analysis reporting among interrupted time series studies in drug utilisation research: a cross-sectional survey. BMC Medical Research Methodology 2024; 24; 62.

57 Kontopantelis E et al. Regression based quasi-experimental approach when randomisation is not an option: interrupted time series analyses. BMJ 2015; 350; h2750.

58 Hudson J, Fielding S, Ramsay CR. Methodology and reporting characteristics of studies using interrupted time series designs in healthcare. BMC Med Res Methodol 2019; 19(1); 137.

59 Morales DR et al. Estimated impact from the withdrawal of primary care financial incentives on selected indicators of quality of care in Scotland: controlled interrupted time series. BMJ 2023; 380; e072098.

60 European Medicines Agency ICH E9[R1] addendum on estimands and sensitivity analyses in clinical trials to the guideline on statistical principles for clinical trials 2020; www.ema.europa.eu\en\documents\scientific-guidelines (accessed 2024-07-25)

61 Kanan BC et al. The estimands framework: a primer on the ICH E9(R1) addendum. BMJ 2024; 384; e076316

62 Bernal J, Soumerai S et al. A methodological framework for model selection in interrupted time series studies. J Clin Epidemiol 2018; 103; 82-91.

63 Bernal J, Cummins S et al. The use of controls in interrupted time series studies of public health interventions. Int J Epidemiol 2018; 2082-2093.

64 Turner S, Karahalios A et al. Design characteristics and statistical methods used in interrupted time series studies evaluating public health interventions: a review. J Clin Epidemiol 2020; 122; 1-11

65 Turner S, Karahalios A et al. Comparison of six statistical methods for interrupted time series studies: empirical evaluation of 190 published series. BMC Medical Research Methodology; 2021; 21(1); 134.

66 Little RJ, D'Agostino R, Cohen ML, Dickersin K, Emerson SS, Farrar JT et al. The prevention and treatment of missing data in clinical trials. N Engl J Med; 367:1355-60.

67 Van Burren. Flexible Imputation of Missing Data, Chapman and Hall, 2018, section 3.8ff

68 Molenburghs G, Kenward M. Missing Data in Clinical Studies, Wiley, 2007; Section 19ff on sensitivity analyses

69 Zhang F, Wagner AK. Simulation-based power calculation for designing interrupted time series analyses of health policy interventions. J Clin Epidemiol 2011; 64; 1252-1261

70 SAS® Institute Inc. SAS for Windows. SAS Institute Inc.: Cary, NC, U.S.A

71 R Core Team (2024). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>.

72 StataCorp 2023. Stata Statistical software Release 18. College Station, TX. StataCorp LLC.