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A study protocol for a national observational cohort investigating frailty, delirium and multimorbidity in older Surgical Patients: The Third Sprint National Anaesthesia Project (SNAP 3)

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Abstract

Introduction

Older surgical patients are more likely to be living with frailty and multimorbidity and experience postoperative complications. The routine management of these conditions in the perioperative pathway is evolving. In order to support objective decision making for patients, services and national guidance, accurate, contemporary data are needed to describe the impact and associations between frailty, multimorbidity and processes of care with patient and service level outcomes.

Methods and analysis

The study is comprised of an observational cohort study of approximately 7,500 surgical patients; an organisational survey of perioperative services and a clinician survey of the unplanned, medical workload generated from older surgical patients. The cohort will consist of patients who are 60 years and older, undergoing a surgical procedure during a five day recruitment period in participating UK hospitals. Participants will be assessed for baseline frailty and multimorbidity; postoperative morbidity including delirium; and quality of life. Data linkage will provide additional details about the patient, their admission and mortality.

The study's primary outcome is length of stay, other outcome measures aim to capture patient or process related metrics including incidence of postoperative morbidity and delirium; readmission, mortality and quality of life. The cohort's incidence of frailty, multimorbidity and delirium will be estimated using 95% confidence intervals. Their relationships with outcome measures will be examined using unadjusted and adjusted multilevel regression analyses. Choice of covariates in the adjusted models will be based on directed acyclic graphs representing hypothesised causal pathways, which will be specified prior to analysis. We will follow the recommendations of the STROBE statement when reporting results.

A parallel study is planned in Australia to take place in 2022/2023.

Ethics and dissemination

The study has received the following approvals: Scotland A Research Ethics Committee and Wales Research Ethics Committee 7. The cohort study requires the participant's consent or a consultee's advice if a participant doesn't have capacity. It is essential to include those who lack capacity, because conditions such as dementia are associated with increased frailty, multimorbidity and delirium.

This work hopes to influence the development of services and guidelines. We will publish our findings in peer reviewed journals and provide summary documents to our participants, recruiting sites, healthcare policy makers and the public.

Registration details

International Standard Randomised Controlled Trial Number 40636, registered 23rd December 2021.

ARTICLE SUMMARY

Strengths and limitations of this study

- The breadth of UK hospital engagement and inclusivity of the study will allow conclusions applicable to countries with similarly developed healthcare systems.
- Inclusion of those without capacity has been encouraged with the use of consultees, this aims to reduce sampling bias of inappropriate exclusion.
- Recruitment will occur over a short period which may result in our dataset not being truly representative of the emergency surgical work carried out across the week.
- We have taken a balanced approach between pragmatism and meticulous identification of outcomes by combining clinical assessment with a retrospective notes review.
- There is a reasonable chance of losing participants to follow up. We have minimised the chances of this occurring by providing email reminders to local investigators; offering email or telephone outpatient follow up to participants and using data linkage to reduce participant burden.

INTRODUCTION

Background

The proportion of people aged 60 years or more undergoing surgery in England increased from 12.6% in 2000, to 17.8% in 2015 [1]. This is due to increased longevity; patient expectations of quality and length of life increasing; and advances in perioperative medicine, anaesthetic and surgical techniques [2].

Many older people benefit from surgery through an increase in longevity or an improvement in symptoms. Yet among surgical patients, older age, frailty and multimorbidity are associated with higher rates of postoperative morbidity, mortality, and adverse patient reported outcomes such as quality of life and loss of independence [3-14]. Frailty is characterised by physiological decline across multiple organ systems with multidomain loss of reserve, resulting in vulnerability to a range of adverse outcomes following a stressor event [15]. Multimorbidity is the presence of two or more co-existing chronic diseases in one individual [16]. The relationship between frailty and multimorbidity and their contribution to postoperative outcome in a surgical setting has not been thoroughly explored to date [17].

Delirium is a state of acute confusion that is commonly reversible and is characterised by fluctuating levels of attention and awareness; disorientation; memory impairment; disturbances of perception; and disorganised thinking [18]. It is one of the most frequently occurring postoperative complications in older adults. It is commonly reversible, and is preventable in approximately 40% of cases [19, 20]. Occurrence of delirium is associated with increased mortality at 12 months, as well as functional and cognitive decline [21, 22].

Frailty and delirium are geriatric syndromes which commonly coexist in older patients, however the details of their relationship is not fully understood. Those who are frail are vulnerable to minor stressors, and so might be expected to more commonly suffer with delirium and other poor outcomes [23, 24]. In a study of older patients recently discharged from hospital, those who were frail were found to be 2.5 times more likely to experience delirium than the corresponding non-frail population [25]. Another study of older vascular patients found that frailty was a strong predictor for delirium with an odds ratio (OR) of 5.66 (95% CI 1.53-21.03) [26]. Intuitively the presence of multimorbidity might also be expected to increase a patient's likelihood of suffering delirium. A study of older patients undergoing elective surgery found a relative risk of 1.75 for delirium in those suffering multimorbidity compared to those without [27].

The influence of frailty on a range of patient outcomes including postoperative quality of life, mortality, morbidity, reoperation, length of stay, readmission and discharge to residential care is widely reported [3, 4, 6, 28-30]. A review of older surgical patients by Lin et al., demonstrated a significant relationship with 12-month mortality, finding an OR of 1.1-4.97 for those living with frailty, compared to patients who were not frail [3, 31, 32]. Two of the studied papers also reported an association with two-year mortality (OR 4.01 (95% CI 2.61-6.16) [32]), and five-year mortality (OR 3.6 (95% CI 2.3-5.5 [33]). The review also highlighted an association between frailty and length of stay [3, 34-37]. This association was further demonstrated in a systematic review of acute surgical patients by Leiner et al. In

this meta-analysis, those living with frailty experienced an increased length of stay with a weighted mean difference of 4.75 days (confidence interval (CI) 1.79-7.71, p=0.002) [29]. A further meta-analysis by Panayi et al. found that surgical patients living with frailty were more likely to experience postoperative complications (relative risk (RR) of 1.48, 95% CI 1.35-1.61, p<0.001), readmission (relative risk 1.61, 95% CI 1.44-1.80, p<0.001) and discharge to skilled care (risk ratio 2.15, 95% CI 1.92-2.40, p<0.001) [30].

Routine assessment and management of frailty, multimorbidity and risk of postoperative delirium can reduce the likelihood of adverse outcomes in older patients [2, 28, 38]. In recent years, the specialty of perioperative medicine has brought together physicians, geriatricians, anaesthetists, surgeons, nurses and allied healthcare professionals, to enhance preoperative assessment; management and postoperative care of these patients. However, the provision of this skilled and specialised service differs across the UK with the varying degrees of resource allocation, local enthusiasm and operational priorities. Furthermore, surgical pathways are heterogenous; often combining proactive and reactive services led by different specialities. The criteria for accessing perioperative medicine services are diverse, based on age, clinical need, surgical specialty, surgical procedure and clinician preference [38-41].

There is no single metric that defines a 'good' outcome following surgery. Length of hospital stay as a metric of outcome has been criticised due to the influence of social and organisational factors. However, these factors are associated with frailty and multimorbidity, and furthermore are important metrics at an organisational and financial level in particular due to an ageing surgical population and resource constraints within healthcare.

In order to support objective decision making for individual patients, services and national planning, accurate, granular and contemporary data are needed describing the impact and association between frailty, multimorbidity and processes of care with patient and service level outcomes.

This study is called the Sprint National Anaesthesia Project 3 (SNAP 3). We have designed it to describe the incidence of and relationships between frailty, multimorbidity and postoperative delirium in the older surgical patient. This protocol will be used across participating UK hospitals. Further research using an adapted SNAP 3 protocol is planned in Australia. From our results we hope to provide suggestions for the future development of perioperative care for the older surgical population.

Objectives

To describe the impact of frailty, multimorbidity and delirium, and their management, on outcomes following surgery in patients aged 60 years and older undergoing surgery.

Primary Objective:

- O1: To describe the prevalence of frailty and multi-morbidity, and the incidence of postoperative delirium in a surgical population aged 60 years or more.

Secondary Objectives:

- O2: To describe the bivariate associations between our three main variables of interest – frailty, multimorbidity, delirium – with a range of patient and process related outcomes.
- O3: To describe the univariate associations between frailty and delirium, as well as multimorbidity and delirium, where delirium is viewed as an outcome.
- O4: To provide an estimate of the effects of frailty, multimorbidity and delirium on primary and secondary outcomes with adjustment for clinically important confounding factors including surgical speciality; surgical acuity; surgical complexity.
- O5: To establish the degree of agreement between three measures of patient frailty: Clinical Frailty Scale, reported Edmonton Frailty Score, and Electronic Frailty Index.
- O6. To estimate proportions of patients who receive more in-depth perioperative interventions, separately for those identified as frail when compared with patients not identified as frail.
- O7: To develop and internally validate a risk prediction model for post-operative delirium.
- O8: To describe the national provision of perioperative medicine services for older people.
- O9: To identify associations between perioperative medicine for older people services and primary and patient reported secondary outcomes.
- O10: To estimate the acute, unplanned workload for general and geriatric medicine registrars generated by acute referrals for older surgical patients.
- O11: To identify associations between hospital level perioperative medicine services and the workload from surgical patients referred to general and geriatrician medical registrars.

METHODS

Study design and setting

The SNAP 3 programme of work consists of three components to be conducted in participating hospitals across the UK:

S1. A five day, prospective, observational cohort study of those who are 60 years and older, undergoing surgery to describe incidence, relationships and outcomes related to frailty, multimorbidity and postoperative delirium.

S2. Organisational survey regarding the provision of perioperative medicine facilities for older surgical patients.

S3. An observational, cross sectional survey of acute referrals from surgical specialities to medicine and the provision of perioperative medicine training.

This protocol will be used in all participating UK sites and has been received favourable opinion from the relevant ethics committees. The study will be replicated in Australia. Due to differing regulations surrounding research, the protocol will be adapted for local implementation outside of the UK and this adaptation will be published separately. Our approach is modelled on the Donabedian framework of structure, process and outcomes [42]. The methodology of the cohort study will be discussed in full below.

Organisational Survey S2:

Each site participating in SNAP 3 will be asked to complete an organisational survey.

This will describe the provision of perioperative medicine services at hospital level. We hope this information will illustrate the range of perioperative medicine services and the differing criteria used to access such services in different centres. One survey is requested per hospital site via the Principal Investigator who could delegate the responsibility to a more appropriate individual if necessary.

Medical Registrar Survey S3:
For a minimum of 24 hours, each general and geriatric medicine registrar (including middle grade trainee or Trust grade equivalents) providing acute medical cover, will be asked to complete a survey on the workload resulting from older surgical patients. The survey will describe brief details of the medical problem, the nature of the review/advice given and any perioperative medicine training they have received. The objective of this survey is to quantify the unplanned workload experienced by general medical registrars and describe associations between existing perioperative medicine services and burden on acute medical services.

Outcome measures
SNAP 3 aims to detect outcomes relevant to professionals, patients and their relatives. We have used multi-level outcome metrics to capture a breadth of informative outcome markers.

Our primary outcome measure is length of stay in hospital after surgery, a well-recognised measure of importance to healthcare services and patients. We recognise that length of stay is influenced both by medical complications and discharge planning issues, both are relevant to frailty, multimorbidity and delirium. A strength of the study is the measurement of outcomes of importance to patients; days alive at home (DAH), days alive out of hospital (DAOH) and quality of life (through us of the EQ-5D-5L and EQ-VAS).

Secondary Outcomes:
Secondary outcomes are important as complementary patient or process-relevant metrics. These have been categorised into patient and process related outcomes, with some crossover between these categories.

Patient Related Secondary Outcomes:

- Delirium incidence during the first seven days postoperatively; measured using 4AT or Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), and retrospective notes review mapped to the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5 criteria for diagnosis of delirium [18, 43-45]
- Morbidity on postoperative days three and seven: measured using the Postoperative Morbidity Score (POMS) [46-48]
- Mortality in hospital and at one, two, five and ten years
- Quality of life at four months postoperatively (measured using the EQ-5D-5L, EQ-VAS)
- Days alive out of hospital (DAOH) and days at home (DAH) [49].

Process Related Secondary Outcomes:

- Number of referrals to acute medical services for older surgical patients, and the rate of such referrals by size of hospital (determined by number of beds).
- Readmission within 30-days of index surgical procedure, estimated using routinely collected hospital data (e.g. HES in England).

Eligibility criteria

Hospital level:

All NHS hospitals in the UK which carry out adult surgery (inpatient, day surgery or both) will be eligible to take part. Hospitals will be recruited through the National Institute of Academic Anaesthesia's Quality Audit and Research Coordinator (QuARC) and national Research and Innovation networks. The QuARC network consists of one or more research- / audit-interested anaesthetists in every NHS hospital who act as a contact, and in many cases also as the local lead investigator for Health Services Research Centre (HSRC) projects. There is also national network of research and innovation support in the UK NHS, which facilitates research support for eligible studies. As a consequence, in previous HSRC affiliated projects there has been near complete recruitment of eligible UK hospitals [50]. We aim to recruit >95% of eligible NHS hospitals for SNAP 3, but accept that this may be challenging due to the impact of SARS-CoV-2 on workforce and theatre operating.

Patient level:

Our inclusion criteria are deliberately broad, with the intention of including almost all patients who have surgery with a significant physiological stress response that could result in postoperative delirium or morbidity. Our exclusion criteria are limited and aim to minimise recruitment of participants whose clinical course is unlikely to provide information which answers our research questions.

Inclusion criteria:

Patients aged 60 years or older undergoing surgery during the recruitment period are eligible for this study. Surgery includes day-case, emergency, and elective procedures that require general, neuraxial, regional or local anaesthesia.

Exclusion criteria:

We will exclude patients undergoing invasive procedures that are diagnostic or likely to cause minimal physiological stress response, e.g. endoscopy, phacoemulsification, percutaneous tracheostomy insertion. Patients with American Society of Anesthesiologists Physical Status score grade VI are also excluded. See Appendix 1 for examples of included and excluded surgical procedures.

Data collection and follow up procedures for the cohort study

Recruitment for the SNAP 3 observational cohort study will occur over a five day period (Monday – Friday). The majority of sites are expected to recruit in the main recruitment window in March 2023. Allowance has been made for sites unable to recruit in the March window to recruit within 2 months. If we are unable to achieve our recruitment target, ethical approval has been given for a second recruitment period. Follow up involving direct participant contact will occur up to four months postoperatively. Data linkage with hospital records and ONS death registrations will be carried out at 120 days after discharge and at one, two, five and ten years postoperatively.

All sites will use an electronic Case Report Form (CRF) via a secure web-based portal 'REDCap'. An initial CRF record will be completed for each participant during the study week. The CRF includes routinely collected demographics, medical history, surgical information, blood laboratory data, SARS-CoV-2 status, surgical risk scores, socioeconomic data and frailty assessments. Please see Appendix 2 for details of the data points collected.

There are two active frailty tools that require participant involvement and one passive frailty score. The Clinical Frailty Scale (CFS) and the Reported Edmonton Frailty Score (rEFS) are both brief and validated methods that do not require specifically trained personnel to accurately assess frailty. The electronic Frailty Index (eFI) operationalises the deficit accumulation model of frailty but is not available in all areas of the UK. It is calculated from Primary Care data. The eFI will be recorded if it has been routinely collected. Those carrying out frailty assessments were given details of relevant online training modules [51, 52]. The conventional cut off values for frailty will be used in analyses. Frailty will be identified as CFS ≥5, rEFS ≥8 and eFI ≥ 0.25 [28, 53, 54]. The choice of frailty tools aims to first, accurately measure frailty in this sample and second, describe the routine usage of different frailty tools across the four nations of the UK [53-59].

Process of care data will be recorded regarding the nature of preoperative assessment, anaesthesia type, catheterisation and postoperative care level.

Multimorbidity is assessed through a list of relevant comorbidities which has been derived from the Charlson Comorbidity Index and a priori knowledge of comorbidities relevant to older patients with frailty and at risk of delirium [60]. The Elixhauser comorbidity index will be calculated from HES data (or equivalent) following the method of Pritchard et al including a one-year look back [61].

Participants who remain inpatients on days three and seven will be assessed for postoperative morbidity using an appropriate speciality specific POMS and either the 4AT (if not critically ill) or CAM-ICU (if critically ill) [45-48, 62]. Delirium and postoperative morbidity will be assumed absent for those discharged alive on the day of surgery.

Those admitted for one or more nights will have a retrospective notes review to identify delirium with the aim of minimising false negatives from researcher assessments alone. This will include medical and nursing documentation, from the day of surgery, up to discharge or day seven postoperatively, whichever is sooner. A tool has been developed to enable objective researcher led retrospective notes evaluation. The tool was developed using DSM-5 criteria for a diagnosis of delirium based on literature review and a priori knowledge of language used by clinicians to describe delirium [63-68]. . Each diagnostic criterion from DSM-5 has been mapped to a set of words and phrases which are commonly used to describe that specific clinical feature.

We aim to minimise the number of missed delirium episodes by combining the findings of the notes review and POMS with either the 4AT or CAM-ICU. This pragmatic approach to the identification of delirium is proposed due to the inherent difficulty in measuring a fluctuating condition with limited resource.

Quality of life will be assessed via email or telephone follow up at 120 days after surgery. The mode of follow up is determined by the participant or their representative. If a participant or their representative has opted into both email and telephone follow up but does not respond to email, the local investigator will be emailed to prompt a telephone call. The EQ-5D-5L and EQ-VAS are validated tools that do not require specific training for accurate use [69]. We will also determine the 'days at home' (DAH) and 'days alive and out of hospital' (DAOH) at 120 days as a measure of the process of recovery that has been shown to be of importance to patients [70]. Days alive and out of hospital is available from central records, and hence easier to collect at scale, but excludes time in residential or nursing home care, outcomes which are often feared by older patients. Days at home, is more difficult to capture, but more closely aligns with what patients want from a good recovery. A possible by product of the study is a demonstration of whether the collection of DAH is worth the additional research burden.

Data linkage via national government held and hospital level datasets will enable us to provide more detailed outcome data without further patient or Local Investigator burden. We will collaborate with NHS Digital, Digital Health and Care Wales, Electronic Data Research and Innovation Service, National Services Scotland and individual Northern Irish hospitals to provide as much of the long-term outcome data as possible. Due to individual countries differing legislation and record keeping, data obtained will vary across the devolved nations.

Data collection for the clinician surveys

The organisational survey, S2 will be distributed via email with a direct link to the REDCap data entry portal. S3 will be administered by researchers (anaesthetists, physicians or research nurses), who will contact medical registrars at the end of an on-call shift. This may be done over the telephone or face to face. The researcher will input their answers directly into REDCap. There will be no ongoing follow up of clinicians.

Analysis plan

Study Cohort:

Descriptive statistics will be used to describe the basic demographics of our participants and key features of our participating sites.

Missing Data:

As with any large study with multiple follow up surveys, there will be missing data. The number and proportion of missing observations will be documented in each analysis. For each variable, we will assess the likely process that led to missing data, to determine whether the data are missing at random or not missing at random. This will determine the choice of an appropriate method of dealing with missing data, for example multiple imputation.

Analysis per objective:

Objective 1: Estimating the incidences of frailty, multimorbidity and postoperative delirium

We will estimate the incidences of our three target variables as the proportion of patients living with frailty and /or multimorbidity, and who experience delirium, respectively. We will

calculate 95 % confidence intervals using the binomial distribution. We will conduct sensitivity analyses with inverse probability weights for elective and emergency procedures in order to account for the absence of weekend data. We have already obtained estimates of the number of emergency and selective procedures carried out at weekends from selected hospitals, and will use those to estimate the inverse probability weights.

Objective 2 & 3: Bivariate analyses

The relationships between frailty, multimorbidity, delirium, primary and secondary outcomes will be reported with appropriate models chosen for different outcome types: multilevel logistic quantile or linear regression. We will account for clustering of patients in hospitals through a random effect for hospitals within mixed-effects models.

Objective 4: Multilevel regression models

To investigate the relationships between frailty, multimorbidity, delirium and a range of outcomes, we will use multilevel regression models adjusting for other clinically relevant preoperative patient characteristics and type of surgery, with hospital-level random intercepts to control for potential between-hospital differences in outcomes. Appropriate models will be chosen for different outcome types: multilevel logistic regression for binary outcomes, multilevel quantile regression for length of stay, DAOH and DAH, and multilevel linear regression for the EQ-5D utility index. Prior to conducting these analyses, we will draw directed acyclic graphs to clarify hypothesized causal relationships and to inform choices of potential covariates that should be included, or indeed excluded, from our models.

Objective 5: Agreement between frailty tools

The analyses for objectives 1-3 will be reported separately for the different frailty measures to gauge differences in their performance as predictors of outcome, using a range of measures of performance as appropriate for the measurement levels of the various outcomes [71]. We won't do the same for the multivariable analyses specified to address objective 4. We will measure the pairwise consistency between the three frailty measures using Spearman's correlation coefficients. To gauge agreement of clinical judgement in practice, we will also assess agreement between dichotomized versions of the three frailty measures, using their respective conventional cut-offs. Agreement between dichotomized frailty measures will be assessed via percentage agreement and kappa coefficient.

Objective 6: Descriptive statistics of interventions

To address the objectives relating to hospital-level and patient-level interventions and perioperative care designed to address risks associated with patient frailty, we will study the sample of patients identified as living with frailty preoperatively and compare them to those identified as not frail. We will document between-hospital differences in interventions and procedures, using descriptive statistics and graphical methods.

Objective 7: Risk prediction model for delirium

Development and internal validation of a risk prediction model for delirium will involve the following steps: (1) Exploratory and graphical analysis of the shapes of the relationships between (numeric) candidate predictors, identified from previous studies and clinical insight, and the probability of delirium. (2) Use of fractional polynomials or splines to identify suitable transformations of numeric predictors, as appropriate. (3) Penalized logistic regression will

be considered for predictor selection, since these have been shown to outperform maximum likelihood estimation and backward selection procedures in the development of risk models [72]. (4) The discrimination of the risk model will be assessed using the C-statistic (area under the ROC curve), which is to be estimated using optimism correction via bootstrapping [73]. We will also calculate the Brier score and investigate model calibration, using graphical displays and the Hosmer-Lemeshow goodness-of-fit statistic. We will follow the TRIPOD statement in reporting the development and internal validation of the risk prediction model for delirium [74].

Objective 8: Descriptive statistics of hospital level models of perioperative care

The national provision of hospital level perioperative medicine services will be described. The description will be sub-divided into care for elective and emergency patients; and degree of preoperative and postoperative services.

Objective 9: Associations between in-depth perioperative interventions and outcomes

The role of in-depth perioperative interventions in modifying the risk of adverse outcomes in patients with frailty will then be assessed using appropriate mixed effects models as for objective 4. Patient-level covariates, such as age, socioeconomic status etc. will be included as appropriate to distinguish the influence of population characteristics with hospital-level perioperative interventions. Although there is inevitably a risk of significant unmeasured confounding it is difficult to estimate the direction or magnitude of these effects.

Objective 10: Acute referrals to medicine from older surgical patients

Descriptive statistics will be used to describe the number and nature of acute referrals to medicine from older surgical patients, and the rate of such referrals by size of hospital (determined by number of beds). The nature of the referrals will be reported as resulting in a telephone or face to face consultation. Referrals will be categorised by surgical speciality, urgency of surgery and primary medical problem.

Objective 11: Identify associations between perioperative medicine services and acute referrals of older surgical patients to medicine

To describe the associations between perioperative medicine services and acute referrals of older surgical patients to medicine, we will use mixed effects logistic regression. Patient level covariates will be included as appropriate to distinguish the relevant perioperative services. Emergency surgery patients will not benefit from an elective perioperative medicine service and so will be analysed separately.

Subgroup analyses:

Data will be reported according to pre-specified subgroups for objectives 1-6. Exact details of subgroups will be finalised once the numbers of patients in potential groups is known. At a minimum the following groups will be reported:

- Emergency and elective procedures
- Surgical invasiveness (using the method described by Abbot et al. [75])
- Major surgical specialty (e.g. orthopaedics, gynaecology)
- The 10 most common healthcare resource groups

Relevant subgroups will be analysed if they include at least 500 participants

Additional analyses and data sharing:
Investigators from outside the core study team may wish to conduct secondary analysis of the data from SNAP 3. We recognise the importance of sharing data within the ethical and legal constraints of the original participants' consent, in order to maximise the potential of our dataset. Following a formal request for data sharing, the request will be considered by the SNAP 3 Study Management Group (SMG) and Steering Committee. If the request is made after the relevant groups have been disbanded, then the request will go directly to the Chief Investigator who will consider the request alongside the Executive Management Board of the HSRC.

There are many potential further analyses possible from the SNAP 3 dataset. We anticipate developing and validating a multimorbidity score for our population. This will then be compared with other measures of multimorbidity to evaluate its ability to predict primary and secondary outcomes. Our secondary analysis plans will continue to evolve as we understand the potential of our cohort's data.

Sample size calculation

Prior to the SARS-CoV-2 pandemic, the estimated achievable sample size for the observational cohort study was around 12,000 participants based on English national data (HES) and previous SNAP projects. We verified that this is a sufficient sample size to achieve the primary and secondary objectives of this study. This estimate has been reduced to 8,000, in light of the impact of the pandemic on health services.

To estimate the proportion of patients living with frailty, and the proportion of patients who develop delirium, a sample size of 7,203 is needed for a margin of error of 1 percentage point (width of 95 % confidence interval: 2 percentage points). This calculation is based on an outcome proportion of 0.25, which is a plausible conservative upper bound. The true proportions are likely to be smaller, which would yield greater precision of the estimation of the true proportion.

To estimate required sample sizes for the delirium risk prediction model, we followed methods published by Riley et al [76]. We made the following assumptions:

- The number of candidate parameters in the risk prediction model is at most 30
- The proportion of patients with delirium is at least 0.05, and at most 0.25
- The Cox-Snell R-square of the prediction model is at least 0.05

These are conservative assumptions. Using the most conservative assumptions in each calculation, the required sample sizes for the following desirable quality criteria are:

- Mean absolute error of predicted probabilities <= 0.01: n = 11,077
- Shrinkage during model development using penalized regression methods <= 5 %: n = 5,395
- Overoptimism of model performance <= 1 %: n = 8,909

These are strict quality criteria, and they suggest that a sample size of around 11,000 patients is sufficient to estimate a high-quality clinical prediction model for delirium.

To achieve the objectives relating to hospital variation in, and effects of, processes and procedures for treating patients with frailty, we plan to estimate multivariate mixed effects

models. There is no precise method for sample size calculations for these kinds of analyses. A conservative lower bound of the percentage of patients with frailty in our achieved sample is 10 %, which implies a minimum sample size of 1,200 patients with frailty. This will give these analyses meaningful precision even in the presence of many covariates.

A priori subgroup analyses will be defined in the statistical analysis plan that will be published separately before data-lock.

ETHICS AND DISSEMINATION

The study has received the following approvals: Scotland A Research Ethics Committee and Wales Research Ethics Committee 7. Ethical approvals are obtained at national level. Local confirmation of capacity and capability is provided by individual hospitals before study commencement.

Patient Consent

All patients who are eligible for SNAP 3 inclusion will have capacity to consent assessed. Those who have capacity to consent to study participation will provide electronic or written consent after being provided with the Participant Information Sheet.

It is essential to include participants without capacity to consent to study participation in order to minimise sampling bias due to exclusion of the target population. The objectives of SNAP 3 relate directly to patients who have both acute and chronic cognitive impairment. This study is of low participant burden and the new knowledge generated will improve care for those without capacity. We will use the process of consultees (in England, Northern Ireland and Wales) and Personal Legal Representatives (PLR, in Scotland) giving advice or consent respectively.

Patient participants who lose capacity to consent:
We anticipate that a proportion of participants will lose capacity to consent during the study, most commonly due to delirium. Whilst it is vital to continue including these participants to fulfil our research objectives, their continued inclusion is complex, and procedures vary depending on the country.

England and Wales:
Those who lose capacity to consent will be treated in accordance with section 34 of the Mental Capacity Act (2005). Information gathered about the participant before loss of capacity will continue to be used in the study. If further interventions are required, then advice will be sought from a consultee for them to continue in the study.

Northern Ireland and Scotland:
Those who lose capacity to consent in Northern Ireland will be treated in accordance with section 132 of the Mental Capacity Act (NI 2016). In the event that a previously consenting participant loses capacity, their statement will still stand unless subsequently withdrawn. In Scotland there is no specific legal provision for those who develop incapacity during research studies. It is generally accepted practice to inform those consenting that they will continue to be included in the study even if they develop incapacity.

Regardless of capacity, if a participant is distressed by ongoing inclusion in the study then they will be withdrawn from the study.

Study management

The SMG is chaired by the Chief Investigator and meets at least monthly, to direct day to day running of the project. The SMG members include those with clinical roles in anaesthesia and geriatrics, a statistician, research management and PPI members. The Study Steering Committee (SSC) meets at least annually to supervise the conduct of the research and its progress achieving the study's objectives whilst working to the protocol. We are fortunate to have multidisciplinary input from all interested clinical groups and lay representation. We are responsible to the HSRC Executive Management Board. The study sponsor is the University of Nottingham.

Patients and public involvement

The topic for SNAP 3 was selected through a competitive process of submissions open to all anaesthetists across the UK. The panel for project selection included representatives from patient and public involvement (PPI) groups, Royal College of Anaesthetists staff, clinicians and trainees.

Our PPI members have provided valuable input into the design and conduct of the study via the SMG and the SSC. They have been influential in the selection of outcome measures especially relating to quality of life. Our PPI members have directly contributed to the format and wording of the patient facing documentation and communication with sites. They have also provided guidance on the acceptability of our study design in relation to participant burden. PPI members will be involved in the publication of our results through our dissemination plans and the production of future public facing documents.

Dissemination

We intend to present the results via our website (hosted by the HSRC), in peer reviewed journals and through conference presentations. We will provide relevant summary reports for the following groups:

1. Our participants- participants will be offered the opportunity to receive summary findings up to three years after recruitment.
2. Our recruiting sites- all sites can receive an overall summary and can request a hospital specific summary.
3. Healthcare policy makers- this will include medical and nursing royal colleges, specialist societies, Department of Health, NHS England, NHS Wales, NHS Scotland and Health and Social Care Ireland.
4. The public- relevant patient groups and charities will be informed of our results with the assistance of our PPI members.
5. Participating NHS Trusts and Health Boards- all NHS Chief Executives will receive a summary of the key findings.

All collaborators who recruit or collect data from participants, or complete clinician surveys will be acknowledged in the manuscripts that arise from this study. Full details can be obtained on our website.

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AUTHORSHIP STATEMENT

The following are members of the SNAP 3 Project Team: Iain Moppett (Co-chief Investigator, UK), Judith Partridge (Co-chief Investigator, UK), Thomas Poulton (Chief Investigator, Australia), Peter Martin (Study Statistician) and Claire Swarbrick (Trainee Lead, UK).

CONTRIBUTOR STATEMENT

IM initiated the collaborative project; is guarantor; the grant holder; revised the draft paper; cowrote the analysis plan and is analysing the data. CS obtained ethical approval; implemented the study in the UK; designed the data collection tools; monitored data collection for the study; cowrote the statistical analysis plan; cleaned and is analysing the data; and drafted and revised the paper. PM provided statistical expertise in study design and cowrote the analysis plan. JP provided expertise in geriatric medicine; designed data collection tools and revised the draft paper. TP implemented the study in Australia; designed data collection tools and revised the draft paper.

Karen Williams, Christine Taylor, Laura Courtes and Jose Lourtie provided organisational support throughout the study's conception, design phase and implementation. Karen Williams managed the day to day administrative needs of the project. Bob Evans and Carol Green are lay representatives who have provided their expertise into the design and implementation of the study. Akshay Shah provided expertise in perioperative medicine and designed data collection tools. The SNAP 3 Local Investigators provided the data (a full list of contributors will be published with the results paper).

All members of the SNAP 3 Project Team designed the study.

COMPETING INTERESTS

The authors declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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DATA STATEMENT

The data from the SNAP 3 study will be published in a data repository.

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Appendix 1: SNAP 3 Examples of Included and Excluded Procedures

This list contains examples of included and excluded procedures for SNAP 3. We hope that it will be useful when making decisions regarding whether a participant should be approached for the study. It is not designed to be comprehensive, most surgical procedures are included. We have tried to not include the very minor procedures but it is challenging to know where to draw the line. We hope this guidance is useful.

Ophthalmology

Include	**Exclude**
Corneal grafts	Any procedure under topical anaesthesia
Scleral buckle	LASER (cornea, medical retina)
Eyelid reconstruction	Adnexal (eyelid surgery inc. ptosis, blepharoplasty)
Keratoplasty	Removal of oil from vitreous body
Excision of scalp/skin lesions **if require a split skin graft (SSG) or flap**	Excision of scalp/skin lesions **not requiring a SSG or flap**
Vitreoretinal surgery	Superficial eye lid surgery
Strabismus surgery	Vitrectomy using pars plana approach
Enucleation/eviscerations/orbital decompression	Correction of entropion of lower eyelid
Radioactive plaque insertion & removal	Dacryocystorhinostomy
Tantalum markers	Cataract surgery
Glaucoma surgery	Removal of sutures
Anterior orbitotomy	Needling
Trabeculectomy	Preserflo microshunt & mitomycin-C
Retinal surgery anaesthesia	Cataract surgery (regardless of anaesthesia mode)

General Surgery

Include	**Exclude**
Inguinal hernia repair under local anaesthesia +/- sedation	Lymph node biopsy
VAC dressing change	Simple dressing change
Perianal excision of rectal polyp	Diagnostic and therapeutic endoscopy regardless of anaesthesia mode
EUA rectum	
Manual evacuation	
Axillary clearance	
Oesophageal dilation/stenting	

ENT

Include	Exclude
Excision of larger lesions e.g basal cell carcinoma (BCC)/squamous cell carcinoma (SCC) **e.g. requiring more than primary closure, SSG/flap.** NB. Mode of anaesthetic here does not influence decision	Excision of smaller BCC/SCC **e.g. no SSG/flap required.** NB. Mode of anaesthetic here does not influence decision
Microlaryngoscopy	Biopsy of tongue
Minimally invasive parathyroidectomy	Frenuloplasty
Manipulation or examination under anaesthetic nose	Removal salivary tube
Cervical lymph node biopsy if GA	Tracheostomy insertion/change
Panendoscopy	Grommets
	Anaesthesia for diagnostic procedures
	Tracheo-oesophageal puncture
	Thyroplasties
	Tracheostomy insertion/change

Thoracics

Include	Exclude
Diagnostic bronchoscopy if with other procedure	Endobronchial ultrasound (EBUS)
Tracheal stenting	Diagnostic bronchoscopy alone
Rigid bronchoscopy	Diagnostic and therapeutic bronchoscopy/pleuroscopy
Mediastinoscopy	Chest drain as sole procedure
Video assisted thoracoscopic surgery (VATS)	
Endoscopic procedures performed ancillary to surgical procedure ○ Bronchoscopy prior to lung resection	

Cardiac

Include	Exclude
Transcatheter aortic valve implantation (TAVI)	Ablations
Other minimally invasive valve replacement procedures carried out under general anaesthesia	PPM lead extractions
	Angiography, percutaneous coronary intervention (PCI)

	Insertion of permanent pacemaker (PPM) / implantable cardioverter defibrillator (ICD)
	Cardioversion
	Electrophysiology (diagnostic or therapeutic)
	Insertion of intra-aortic balloon pump (IABP)

Hands

Include	**Exclude**
	Carpal tunnel decompression under local anaesthetic
	Dupuytren's palmar fasciectomy
	Trigger finger release
	Excision of hand lesion if small

Trauma & Orthopaedics Emergency Department

Include	**Exclude**
Ulnar nerve transposition	Aspiration of knee under local anaesthetic
Removal of metal work	Cheilectomy
Excision of olecranon bursa	Trigger point injections
Vertebroplasty	Therapeutic epidural injection
Trapeziectomy	Intra-articular joint injections
Knee replacement	Dupuytren's fasciectomy
Osteotomy of any bone	MUA joint
Replacement of hip joint	MUA fracture in ED
Replacement of shoulder joint	General anaesthesia/sedation for scanning/ICU management only
Small joint fusion	Post-arrest management
Insertion K wire	Erector spinae catheters
MUA fracture in theatre	Joint injections
Surgery for trauma	Joint aspiration
MUA fractures/dislocations in theatre	
Joint washout	

Urology

Include	**Exclude**
Rigid cystoscopy	Flexible cystoscopy
Urethral dilatation	Circumcision under local anaesthetic
Transurethral resection of bladder tumour	Standard circumcision under general anaesthetic
Transurethral resection of prostate	Transperineal prostate biopsy

Hydrocele under general anaesthetic	Flexible ureteroscopy
Laser fragmentation of stone	Cystoscopy under local anaesthesia
Nephrostomy	Prostate brachytherapy
TURP/TURBT	
Rigid diagnostic/surveillance cystoscopy	
Stent change	

Vascular

Include	**Exclude**
Fistula ligation and banding	Varicose veins under local anaesthetic
Fistula creation	
Endovascular aneurysm repair (EVAR)	

Interventional Radiology

Include	**Exclude**
EVAR	CT guided biopsies
Angioplasty	IV access/line insertion
CT guided drain	Endoscopic retrograde cholangiopancreatography (ERCP)

Dental

Include	**Exclude**
Extractions	

Gynaecology

Include	**Exclude**
Therapeutic hysteroscopy	**Diagnostic** hysteroscopy +/- biopsy
Laparoscopic hysterectomy	Hysteroscopy and smear
Cervical polypectomy	

Neurosurgery

Include	**Exclude**
Sympathetic nerve stimulator insertion or removal	SNS battery or lead change
Spinal cord stimulator insertion	SNS reprogramming
	SCS trial if purely percutaneous

Appendix 2: SNAP 3 Case Report Form

Below are the questions used in REDCap for the SNAP 3 study. For brevity, previously published, validated tools have not been replicated in this document. References for tools used in the SNAP 3 study can be found in the reference list of our accompanying paper.

1.0	**Participant details**				
1.1	Which country is your hospital based in?	England	Northern Ireland	Scotland	Wales
1.2	Which hospital site are you completing this form for?				
1.3	Is the potential participant having surgery AND 60 years or above?	Yes		No	
1.4	What is the planned date of surgery?				
1.5	Does the potential participant have the capacity to consent?				
1.6	Is there a consultee/Personal Legal Representative (PLR) to offer advice? This may be face to face or over the telephone.	Yes		No	
1.7	Is the participant's Consultee (England, Wales and Northern Ireland) or Personal Legal Representative (Scotland) available in person or over the telephone?	Yes		No	
1.8	Participant first name				
1.9	Participant surname				
1.10	Participant date of birth				
1.11	Participant NHS/CHI/H&C number				
1.12	Would the participant/Consultee/PLR be able to complete a survey at 4 months by email or telephone?	Yes by email	Yes by telephone	No	
1.13	Email address				
1.14	Telephone number				

2.0	**Frailty assessment**				
2.1	At any point during the participant's clinical pathway, were they assessed for frailty?	Yes		No	
2.2	Which frailty tool was used to assess the participant?	Clinical Frailty Scale /Rockwood Frailty Scale	Edmonton Frailty Scale (scored out of 17)	Reported Edmonton Frail Scale (scored out of 18)	Groningen Frailty Indicator
		Gait Speed Test	PRISMA-7	Risk Analysis Index-C	Timed Up and Go (TUG) Test
		Electronic Frailty Index	Hospital Risk Frailty Index	Grip Strength	Comprehensive Geriatric Assessment
2.3	What was the result of the frailty tool?				
2.4	Clinical Frail Scale (as completed by the clinical or research team)	1-9			
2.5	Reported Edmonton Frail Scale (as completed by the clinical or research team)	0-18			
2.6	Electronic frailty index	0-36			
3.0	**Demographics and ADLs**				
3.1	Postcode				
3.2	Ethnic group	Census categories			
3.3	Highest level of education	Degree level eg. degree, NVQ Level 4-5, Higher National Certificate, Higher National Diploma, BTEC Higher Level, professional	2+ A levels/VCEs, 4+ AS Levels, Higher School Certificate, NVQ Level 3, Advanced GNVQ, City and Guilds Advanced Craft, BTEC National, Scottish Higher	Apprenticeship	5 or more O Levels (passes)/CSEs (grade 1), School Certificate, 1 A Level, 2-3 AS Levels/VCEs, NVQ Level 2, Intermediate GNVQ, City and Guilds Craft, BTEC, Scottish Higher,

		qualifications (eg. teaching or nursing) or other equivalent higher education qualifications	National Diploma, Scottish Higher National Certificate, SVQ level 4+) or equivalent		Scottish Advanced Higher or equivalent qualifications
		O levels/CSEs (any grade), Foundation Diploma, NVQ level 1, Foundation GNVQ, O grade, Scottish Standard Grade or equivalent qualifications	No formal qualifications	Don't know	
3.4	Biological sex	Female		Male	
3.5	Weight				
3.6	Height				
3.7	BMI				
3.8	Source of admission	Own home	Sheltered housing, retirement complex	Residential home	Nursing home
		Rehabilitation facility (inpatient community unit or care home with the purpose of short term rehabilitation)	Homeless	Another secondary care hospital	Other, please specify

3.9	Help with activities of daily living (ADLs)	No, the participant receives no help with ADLs or the participant has help for lifestyle reasons only (would easily be able to do the tasks if needed).	Needs help with any of the following: transportation, shopping, managing finances, shopping, meal preparation, house cleaning, managing communication with others, managing medications.	Needs help with any of the following: ambulating, feeding, dressing, personal hygiene, continence, toileting.	
4.0	**Preoperative assessment**				
4.1	How was the participant assessed preoperatively?	Nurse (or AHP) led assessment on day of surgery only	Anaesthetist led assessment on day of surgery only	Nurse (or AHP) led clinic	Anaesthetist led clinic
		Physician (non geriatrician) led clinic	Geriatrician led clinic	MDT clinic	Other
		None of the above			
4.2	Urgency of surgery as per NCEPOD criteria	Emergency	Urgent	Expedited	Planned
4.3	Indication for surgery	Confirmed cancer	Possible cancer e.g. surgery with the aim of diagnosing possible cancer	Non-cancer	
4.4		ASA I	ASA II	ASA III	ASA IV

	Which ASA score would you give the participant?	ASA V			
4.5	Surgical Outcome Risk Tool (SORT) Version 2 (including procedure type and surgical speciality, as completed by the clinical or research team)				
5.0	**Comorbidities**				
5.1	Does the participant have any of the following comorbidities?	MI (history of MI based on patient history, notes, history of stent	Heart failure (dyspnoea that has responded to heart failure treatment)	AF (paroxysmal/permanent AF, not if successfully ablated)	Valvular heart disease
		Hypertension (even if treated, do not include those with one isolated episode)	Peripheral vascular disease (treated and untreated)	COPD (probable clinical diagnosis)	Other chronic lung disease
		OSA/obesity hypoventilation syndrome (symptomatic, not purely positive STOP-BANG)	Cerebrovascular disease with mild or no residual symptoms (includes TIA, intracerebral/subarachnoid haemorrhage and stroke diagnosed on CT with no symptoms)	Hemiplegia or paraplegia (from any cause)	Dementia
		Mild cognitive	Anxiety or depression	Parkinson's disease	Diabetes (not just

		impairment	(on treatment)	or parkinsonism	impaired glucose tolerance or if in remission)
		Moderate or severe renal disease (acute or chronic, stage 3A+, eGFR< 60)	Benign prostatic hypertrophy (can be self reported)	Liver disease (with or without portal hypertension)	Peptic ulcer disease (even if treated and not symptomatic)
		Malignancy	Lymphoma (of any type, acute or chronic)	Leukaemia (of any type, acute or chronic)	Connective tissue/rheumatological disease (systemic lupus erythematosus, polymyositis, mixed connective tissue disease, polymyalgia rheumatica, psoriatic arthropathy or rheumatoid arthritis)

		Osteoarthritis (include self reported)	AIDS	Hearing impairment (uses hearing aids or struggles to manage a conversation at usual volumes of speech)	Visual impairment (registered partially sighted)
5.2	Does the participant have complications from their diabetes?	Diabetes without chronic complication		Diabetes with chronic complication	
5.3	How severe is the participant's liver disease?	Mild liver disease (without portal hypertension)		Moderate or severe liver disease (with portal hypertension)	
5.4	Which type(s) of malignancy does the participant have/has had?	Any solid malignancy without metastases		Metastatic solid tumour	
5.5	When was participant's malignancy/malignancies first diagnosed?	≤ 5 years ago		> 5 years ago	
6.0	Investigations within 12 weeks				
6.1	Haemoglobin g/L				
6.2	White cell count 10^9/L				
6.3	Neutrophil 10^9/L				
6.4	Lymphocyte 10^9/L				
6.5	Sodium mmol/L				
6.6	Potassium mmol/L				
6.7	Creatinine micromol/L				
6.8	eGFR ml/min/1.73^2				

6.9	What is the participant's SARS-Cov-2 status preoperatively?	Tested positive or not tested and treated as positive	Tested negative or not tested and treated as negative	Don't know	
7.0	Day of procedure				
7.1	Date of operation				
7.2	Type of anaesthesia	General anaesthesia with volatiles	General anaesthesia with total intravenous anaesthesia (TIVA)	Neuraxial	Regional
		Sedation	Local infiltration	Don't know	
7.3	Was the participant catheterised?	No	Long-term/pre-admission catheter	Electively catheterised pre/intra-op	Catheterised post-op
7.4	What level of care did the participant receive postoperatively (on the day of surgery)?	Ward (level 0 or 1 care, including day case units)	Unplanned admission to PACU or equivalent (level 1.5 care)	Unplanned admission to PACU or equivalent (level 2/3 care)	Unplanned critical care admission (level 2 or 3 care)
		Planned admission to PACU or equivalent (level 1.5 care)	Planned admission to PACU or equivalent (level 2/3 care)	Planned critical care admission (level 2 or 3 care)	Don't know
7.5	Was the participant a day case patient who has been successfully discharged?	Yes, they have been discharged on the day of surgery	No, they are planned to be an inpatient OR they were intended to be day case but haven't been	Don't know	

			discharged on the day of surgery		
8.0	Day 3 follow up				
8.1	Postoperative Morbidity Survey (general/cardiac/fractured neck of femur, as completed by the research team)				
8.2	Documented new confusion or delirium	Yes		No	
8.3	4AT (if the participant isn't critically unwell, as completed by the clinical or research team)	0-12			
8.4	CAM-ICU (if the participant is critically unwell, as completed by the clinical or research team)	Negative		Positive	
8.5	Does the participant recall any symptoms of postoperative delirium or 'acute confusion'?	Yes		No	
9.0	Day 7 follow up				
9.1	Postoperative Morbidity Survey (general/cardiac/fractured neck of femur, as completed by the research team)				
9.2	Documented new confusion or delirium	Yes		No	
9.3	4AT (if the participant isn't critically unwell, as completed by the clinical or research team)	0-12			
9.4	CAM-ICU (if the participant is critically unwell, as completed by the clinical or research team)	Negative		Positive	
9.5	Does the participant recall any symptoms of	Yes		No	

	postoperative delirium or 'acute confusion'?				
10.0	Delirium notes review				
	SNAP 3 will use the validated 4AT and CAM-ICU to detect delirium in participants postoperatively. Due to its fluctuating nature, some participants will not be experiencing delirium at the time of their follow up even though they have had delirium. We would like to maximise the likelihood of detecting delirium by undertaking a notes review on day seven in addition to the validated assessment tools. The notes review will provide the study with an impression of whether or not a patient experienced delirium outside of the time of their delirium assessment. Based on existing literature, a notes review is more likely to detect delirium which occurs at night and hyperactive delirium, than a single assessment (such as CAM) alone. The diagnosis of delirium is often not clearly documented in patient's notes. Estimates of previously unrecognised delirium from retrospective notes are variable, ranging from 7-43%. Nursing notes are more likely than medical notes to document the presence of keywords indicating delirium. The use of DSM-V criteria expanded with words describing delirium have been selected based on previous literature and a priori knowledge. Please review the nursing and medical notes as below. Only record evidence from (up to and including) day seven postoperatively. If there is evidence of delirium occurring on day eight, then please do not report this. If you believe that you have identified a current diagnosis of unrecognised delirium from the notes then please pass these concerns to the clinical team. This is a requirement of good clinical and research practice.				
10.1	If the participant has a diagnosis of delirium documented either using a validated tool or as free text documentation of 'delirium' or 'delirious', then please select 'Positive diagnosis of delirium'	Positive diagnosis of delirium	No explicit diagnosis of delirium	Don't know	
	The following questions summarise the DSM-V criteria for the diagnosis of delirium and give examples of words frequently used to describe delirium in the clinical notes.				
10.2	DSM criteria A: Is there any documentation of the following? Inattention, inattentive, distractable Muddled Drowsy, drowsiness	Yes, phrases similar to the ones listed are used in the notes	No	Don't know	

	Unrousable, unresponsive Hypoactive Agitated, agitation Altered mental status Inability to count from 20-1 Inability to recite months of the year backwards				
10.3	DSM criteria B: Is there any documentation of the following? Acute confusion Fluctuating confusion Fluctuation in severity throughout the day Altered mental status, mental status change	Yes, phrases similar to the ones listed are used in the notes	No	Don't know	
10.4	DSM criteria C: Is there any documentation of the following? Confused, confusion Muddled Hallucination, hallucinating Reorientation, reorientated Disorientation, disorientated, Encephalopathy, encephalopathic, Agitated, agitation Inappropriate behaviour Restless, unsettled Aggressive Wandering Refusing observations/ interventions Uncooperative, not cooperating, Pulling lines out Combative Speaking nonsense Paranoid MoCA < 24 AMTS < 7	Yes, phrases similar to the ones listed are used in the notes	No	Don't know	

10.5	DSM criteria D1: Is the participant functioning at their cognitive baseline?	Yes (they are at their neurocognitive baseline according to available sources of evidence)	No	Don't know	
10.6	DSM criteria D2: If delirium is likely, could this disturbance be better explained by a severely reduced level of arousal or coma? *If suffering from delirium, are the participant's symptoms better explained by being severely obtunded, sedated or unconscious with a Richmond Agitation Sedation Scale of 4 or less?*	Yes	No	Delirium not likely	
	Positive diagnosis of delirium from notes review either from:	Documented diagnosis of delirium in notes	DSM criteria responses: Yes to 10.2, 10.3, 10.4 No to 10.5, 10.6		
11.0	4 month follow up				
11.1	EQ-5D-5L				
11.2	EQ-VAS	0-100			
11.3	From when you had your operation, until 120 days after surgery, how many days have you spent in any hospital? Please include any hospital admissions (including your initial admission for surgery) and rehabilitation in hospitals. If you have				

	been out of hospital since the day of surgery and the surgery was day case then write '0'	
11.4	From when you had your operation, until 120 days after surgery, how many days have you spent from home due to convalescing with family/friends/in residential homes. Don't include days spent socialising away from home or hospital admissions here. If you have been at home since the day of surgery and the surgery was day case then write '0'	

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page/Line	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1/L4-6	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2/L10-18	Protocol paper so no results available
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4/L3-P5/L37	
Objectives	3	State specific objectives, including any prespecified hypotheses	P5/L39-P6/L24	
Methods				
Study design	4	Present key elements of study design early in the paper	P6/L26	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P6/L27-P7/L15-37, P8/L39-47	
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P8/L6-L37, P10/L2-22	
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P7/L17-P8/4, P9/L8-P10/L14, see also Appendix 2	Also see CRF appendix
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P9/L8-P10/L22	
Bias	9	Describe any efforts to address potential sources of bias	P3/L6, P3/L13-16, P9/L34-47, P10/L2-5	
Study size	10	Explain how the study size was arrived at	P13/L17-P14-L4	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P9/L15-16, P9/L23-47	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to	P10/L31-	

		control for confounding	P13/L15	
		(*b*) Describe any methods used to examine subgroups and interactions	P12/L38-46	
		(*c*) Explain how missing data were addressed	P10/L36-42	
		(*d*) If applicable, explain how loss to follow-up was addressed	Protocol paper so not possible	
		(*e*) Describe any sensitivity analyses	P11/L1-5	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Protocol paper so not possible.	
		(b) Give reasons for non-participation at each stage	Protocol paper so not possible.	
		(c) Consider use of a flow diagram	Protocol paper so not possible.	Protocol paper so not possible.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Protocol paper so not possible.	Protocol paper so not possible.
		(b) Indicate number of participants with missing data for each variable of interest	Protocol paper so not possible.	Protocol paper so not possible.
		(c) Summarise follow-up time (eg, average and total amount)	Protocol paper so not possible.	Protocol paper so not possible.
Outcome data	15*	Report numbers of outcome events or summary measures over time	Protocol paper so not possible.	Protocol paper so not possible.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Protocol paper so not possible.	Protocol paper so not possible.
		(*b*) Report category boundaries when continuous variables were categorized	Protocol paper so not possible.	Protocol paper so not possible.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Protocol paper so	Protocol paper so

			not possible.	not possible.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Protocol paper so not possible.	Protocol paper so not possible.
Discussion				
Key results	18	Summarise key results with reference to study objectives	Protocol paper so not possible.	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P3/L8-16	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Protocol paper so not possible.	Protocol paper so not possible.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Protocol paper so not possible.	Protocol paper so not possible.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P16/L40-44	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

A study protocol for a national observational cohort investigating frailty, delirium and multimorbidity in older Surgical Patients: The Third Sprint National Anaesthesia Project (SNAP 3)

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A study protocol for a national observational cohort investigating frailty, delirium and multimorbidity in older Surgical Patients: The Third Sprint National Anaesthesia Project (SNAP 3)

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Keywords: frailty, multimorbidity, delirium, anaesthesia, surgery

Abstract

Introduction

Older surgical patients are more likely to be living with frailty and multimorbidity and experience postoperative complications. The management of these conditions in the perioperative pathway is evolving. In order to support objective decision making for patients, services and national guidance, accurate, contemporary data are needed to describe the impact and associations between frailty, multimorbidity and healthcare processes with patient and service level outcomes.

Methods and analysis

The study is comprised of an observational cohort study of approximately 7,500 patients; an organisational survey of perioperative services and a clinician survey of the unplanned, medical workload generated from older surgical patients. The cohort will consist of patients who are 60 years and older, undergoing a surgical procedure during a five day recruitment period in participating UK hospitals. Participants will be assessed for baseline frailty and multimorbidity; postoperative morbidity including delirium; and quality of life. Data linkage will provide additional details about individuals, their admission and mortality.

The study's primary outcome is length of stay, other outcome measures include incidence of postoperative morbidity and delirium; readmission, mortality and quality of life. The cohort's incidence of frailty, multimorbidity and delirium will be estimated using 95% confidence intervals. Their relationships with outcome measures will be examined using unadjusted and adjusted multilevel regression analyses. Choice of covariates in the adjusted models will be prespecified, based on directed acyclic graphs.

A parallel study is planned to take place in Australia in 2022.

Ethics and dissemination

The study has received approval from the Scotland A Research Ethics Committee and Wales Research Ethics Committee 7.

This work hopes to influence the development of services and guidelines. We will publish our findings in peer reviewed journals and provide summary documents to our participants, sites, healthcare policy makers and the public.

Registration details

International Standard Randomised Controlled Trial Number 40636.

ARTICLE SUMMARY

Strengths and limitations of this study

- The breadth of UK hospital engagement and inclusivity of the study will allow conclusions applicable to countries with similarly developed healthcare systems.
- Inclusion of those without capacity has been encouraged with the use of consultees, this aims to reduce sampling bias of inappropriate exclusion.
- Recruitment will occur over a short period which may result in our dataset not being truly representative of the emergency surgical work carried out across the week.
- We have taken a balanced approach between pragmatism and meticulous identification of outcomes by combining clinical assessment with a retrospective notes review.
- There is a reasonable chance of losing participants to follow up. We have minimised the chances of this occurring by providing email reminders to local investigators; offering email or telephone outpatient follow up to participants and using data linkage to reduce participant burden.

INTRODUCTION

Background

The proportion of people aged 60 years or more undergoing surgery in England increased from 12.6% in 2000, to 17.8% in 2015 [1]. This is due to increased longevity; patient expectations of quality and length of life increasing; and advances in perioperative medicine, anaesthetic and surgical techniques [2].

Many older people benefit from surgery through an increase in longevity or an improvement in symptoms. Yet among surgical patients, older age, frailty and multimorbidity are associated with higher rates of postoperative morbidity, mortality, and adverse patient reported outcomes such as quality of life and loss of independence [3-14]. Frailty is characterised by physiological decline across multiple organ systems with multidomain loss of reserve, resulting in vulnerability to a range of adverse outcomes following a stressor event [15]. Multimorbidity is the presence of two or more co-existing chronic diseases in one individual [16]. The relationship between frailty and multimorbidity and their contribution to postoperative outcome in a surgical setting has not been thoroughly explored to date [17].

Delirium is a state of acute confusion that is commonly reversible and is characterised by fluctuating levels of attention and awareness; disorientation; memory impairment; disturbances of perception; and disorganised thinking [18]. It is one of the most frequently occurring postoperative complications in older adults. It is commonly reversible, and is preventable in approximately 40% of cases [19, 20]. Occurrence of delirium is associated with increased mortality at 12 months, as well as functional and cognitive decline [21, 22].

Frailty and delirium are geriatric syndromes which commonly coexist in older patients, however the details of their relationship is not fully understood. Those who are frail are vulnerable to minor stressors, and so might be expected to more commonly suffer with delirium and other poor outcomes [23, 24]. In a study of older patients recently discharged from hospital, those who were frail were found to be 2.5 times more likely to experience delirium than the corresponding non-frail population [25]. Another study of older vascular patients found that frailty was a strong predictor for delirium with an odds ratio (OR) of 5.66 (95% CI 1.53-21.03) [26]. Intuitively the presence of multimorbidity might also be expected to increase a patient's likelihood of suffering delirium. A study of older patients undergoing elective surgery found a relative risk of 1.75 for delirium in those suffering multimorbidity compared to those without [27].

The influence of frailty on a range of patient outcomes including postoperative quality of life, mortality, morbidity, reoperation, length of stay, readmission and discharge to residential care is widely reported [3, 4, 6, 28-30]. A review of older surgical patients by Lin et al., demonstrated a significant relationship with 12-month mortality, finding an OR of 1.1-4.97 for those living with frailty, compared to patients who were not frail [3, 31, 32]. Two of the studied papers also reported an association with two-year mortality (OR 4.01 (95% CI 2.61-6.16) [32]), and five-year mortality (OR 3.6 (95% CI 2.3-5.5 [33]). The review also highlighted an association between frailty and length of stay [3, 34-37]. This association was further demonstrated in a systematic review of acute surgical patients by Leiner et al. In this meta-analysis, those living with frailty experienced an increased length of stay with a

weighted mean difference of 4.75 days (confidence interval (CI) 1.79-7.71, p=0.002) [29]. A further meta-analysis by Panayi et al. found that surgical patients living with frailty were more likely to experience postoperative complications (relative risk (RR) of 1.48, 95% CI 1.35-1.61, p<0.001), readmission (relative risk 1.61, 95% CI 1.44-1.80, p<0.001) and discharge to skilled care (risk ratio 2.15, 95% CI 1.92-2.40, p<0.001) [30].

Routine assessment and management of frailty, multimorbidity and risk of postoperative delirium can reduce the likelihood of adverse outcomes in older patients [2, 28, 38]. In recent years, the specialty of perioperative medicine has brought together physicians, geriatricians, anaesthetists, surgeons, nurses and allied healthcare professionals, to enhance preoperative assessment; management and postoperative care of these patients. However, the provision of this skilled and specialised service differs across the UK with the varying degrees of resource allocation, local enthusiasm and operational priorities. Furthermore, surgical pathways are heterogenous; often combining proactive and reactive services led by different specialities. The criteria for accessing perioperative medicine services are diverse, based on age, clinical need, surgical specialty, surgical procedure and clinician preference [38-41].

There is no single metric that defines a 'good' outcome following surgery. Length of hospital stay as a metric of outcome has been criticised due to the influence of social and organisational factors. However, these factors are associated with frailty and multimorbidity, and furthermore are important metrics at an organisational and financial level in particular due to an ageing surgical population and resource constraints within healthcare.

In order to support objective decision making for individual patients, services and national planning, accurate, granular and contemporary data are needed describing the impact and association between frailty, multimorbidity and processes of care with patient and service level outcomes.

This study is called the Sprint National Anaesthesia Project 3 (SNAP 3). We have designed it to describe the incidence of and relationships between frailty, multimorbidity and postoperative delirium in the older surgical patient. This protocol will be used across participating UK hospitals. Further research using an adapted SNAP 3 protocol is planned in Australia. From our results we hope to provide suggestions for the future development of perioperative care for the older surgical population.

Objectives

To describe the impact of frailty, multimorbidity and delirium, and their management, on outcomes following surgery in patients aged 60 years and older undergoing surgery.

Primary Objective:

- O1: To describe the prevalence of frailty and multi-morbidity, and the incidence of postoperative delirium in a surgical population aged 60 years or more.

Secondary Objectives:

- O2: To describe the bivariate associations between our three main variables of interest – frailty, multimorbidity, delirium – with a range of patient and process related outcomes.
- O3: To describe the univariate associations between frailty and delirium, as well as multimorbidity and delirium, where delirium is viewed as an outcome.
- O4: To provide an estimate of the effects of frailty, multimorbidity and delirium on primary and secondary outcomes with adjustment for clinically important confounding factors including surgical speciality; surgical acuity; surgical complexity.
- O5: To establish the degree of agreement between three measures of patient frailty: Clinical Frailty Scale, reported Edmonton Frailty Score, and Electronic Frailty Index.
- O6. To estimate proportions of patients who receive more in-depth perioperative interventions, separately for those identified as frail when compared with patients not identified as frail.
- O7: To develop and internally validate a risk prediction model for post-operative delirium.
- O8: To describe the national provision of perioperative medicine services for older people.
- O9: To identify associations between perioperative medicine for older people services and primary and patient reported secondary outcomes.
- O10: To estimate the acute, unplanned workload for general and geriatric medicine registrars generated by acute referrals for older surgical patients.
- O11: To identify associations between hospital level perioperative medicine services and the workload from surgical patients referred to general and geriatrician medical registrars.

METHODS

Study design and setting

The SNAP 3 programme of work consists of three components to be conducted in participating hospitals across the UK:

S1. A five day, prospective, observational cohort study of those who are 60 years and older, undergoing surgery to describe incidence, relationships and outcomes related to frailty, multimorbidity and postoperative delirium.

S2. Organisational survey regarding the provision of perioperative medicine facilities for older surgical patients.

S3. An observational, cross sectional survey of acute referrals from surgical specialities to medicine and the provision of perioperative medicine training.

This protocol will be used in all participating UK sites and has been received favourable opinion from the relevant ethics committees. The study will be replicated in Australia. Due to differing regulations surrounding research, the protocol will be adapted for local implementation outside of the UK and this adaptation will be published separately. Our approach is modelled on the Donabedian framework of structure, process and outcomes [42]. The methodology of the cohort study will be discussed in full below.

Organisational Survey S2:

Each site participating in SNAP 3 will be asked to complete an organisational survey.

This will describe the provision of perioperative medicine services at hospital level. We hope this information will illustrate the range of perioperative medicine services and the differing criteria used to access such services in different centres. One survey is requested per hospital site via the Principal Investigator who could delegate the responsibility to a more appropriate individual if necessary.

Medical Registrar Survey S3:
For a minimum of 24 hours, each general and geriatric medicine registrar (including middle grade trainee or Trust grade equivalents) providing acute medical cover, will be asked to complete a survey on the workload resulting from older surgical patients. The survey will describe brief details of the medical problem, the nature of the review/advice given and any perioperative medicine training they have received. The objective of this survey is to quantify the unplanned workload experienced by general medical registrars and describe associations between existing perioperative medicine services and burden on acute medical services.

Outcome measures
SNAP 3 aims to detect outcomes relevant to professionals, patients and their relatives. We have used multi-level outcome metrics to capture a breadth of informative outcome markers.

Our primary outcome measure is length of stay in hospital after surgery, a well-recognised measure of importance to healthcare services and patients. We recognise that length of stay is influenced both by medical complications and discharge planning issues, both are relevant to frailty, multimorbidity and delirium. A strength of the study is the measurement of outcomes of importance to patients; days alive at home (DAH), days alive out of hospital (DAOH) and quality of life (through us of the EQ-5D-5L and EQ-VAS).

Secondary Outcomes:
Secondary outcomes are important as complementary patient or process-relevant metrics. These have been categorised into patient and process related outcomes, with some crossover between these categories.

Patient Related Secondary Outcomes:

- Delirium incidence during the first seven days postoperatively; measured using 4AT or Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), and retrospective notes review mapped to the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5 criteria for diagnosis of delirium [18, 43-45]
- Morbidity on postoperative days three and seven: measured using the Postoperative Morbidity Score (POMS) [46-48]
- Mortality in hospital and at one, two, five and ten years
- Quality of life at four months postoperatively (measured using the EQ-5D-5L, EQ-VAS)
- Days alive out of hospital (DAOH) and days at home (DAH) [49].

Process Related Secondary Outcomes:

- Number of referrals to acute medical services for older surgical patients, and the rate of such referrals by size of hospital (determined by number of beds).
- Readmission within 30-days of index surgical procedure, estimated using routinely collected hospital data (e.g. HES in England).

Eligibility criteria

Hospital level:

All NHS hospitals in the UK which carry out adult surgery (inpatient, day surgery or both) will be eligible to take part. Hospitals will be recruited through the National Institute of Academic Anaesthesia's Quality Audit and Research Coordinator (QuARC) and national Research and Innovation networks. The QuARC network consists of one or more research- / audit-interested anaesthetists in every NHS hospital who act as a contact, and in many cases also as the local lead investigator for Health Services Research Centre (HSRC) projects. There is also national network of research and innovation support in the UK NHS, which facilitates research support for eligible studies. As a consequence, in previous HSRC affiliated projects there has been near complete recruitment of eligible UK hospitals [50]. We aim to recruit >95% of eligible NHS hospitals for SNAP 3, but accept that this may be challenging due to the impact of SARS-CoV-2 on workforce and theatre operating.

Patient level:

Our inclusion criteria are deliberately broad, with the intention of including almost all patients who have surgery with a significant physiological stress response that could result in postoperative delirium or morbidity. Our exclusion criteria are limited and aim to minimise recruitment of participants whose clinical course is unlikely to provide information which answers our research questions.

Inclusion criteria:

Patients aged 60 years or older undergoing surgery during the recruitment period are eligible for this study. Surgery includes day-case, emergency, and elective procedures that require general, neuraxial, regional or local anaesthesia.

Exclusion criteria:

We will exclude patients undergoing invasive procedures that are diagnostic or likely to cause minimal physiological stress response, e.g. endoscopy, phacoemulsification, percutaneous tracheostomy insertion. Patients with American Society of Anesthesiologists Physical Status score grade VI are also excluded. See Appendix 1 for examples of included and excluded surgical procedures.

Data collection and follow up procedures for the cohort study

Recruitment for the SNAP 3 observational cohort study will occur over a period (Monday – Friday). The majority of sites are expected to recruit in the main recruitment window in March 2023. Allowance has been made for sites unable to recruit in the March window to recruit within 2 months. If we are unable to achieve our recruitment target, ethical approval has been given for a second recruitment period. Follow up involving direct participant contact will occur up to four months postoperatively. Data linkage with hospital records and ONS death registrations will be carried out at 120 days after discharge and at one, two, five and ten years postoperatively.

All sites will use an electronic Case Report Form (CRF) via a secure web-based portal 'REDCap'. An initial CRF record will be completed for each participant during the study week. The CRF includes routinely collected demographics, medical history, surgical information, blood laboratory data, SARS-CoV-2 status, surgical risk scores, socioeconomic data and frailty assessments. Please see Appendix 2 for details of the data points collected.

There are two active frailty tools that require participant involvement and one passive frailty score. The Clinical Frailty Scale (CFS) and the Reported Edmonton Frailty Score (rEFS) are both brief and validated methods that do not require specifically trained personnel to accurately assess frailty. The electronic Frailty Index (eFI) operationalises the deficit accumulation model of frailty but is not available in all areas of the UK. It is calculated from Primary Care data. The eFI will be recorded if it has been routinely collected. Those carrying out frailty assessments were given details of relevant online training modules [51, 52]. The conventional cut off values for frailty will be used in analyses. Frailty will be identified as CFS ≥5, rEFS ≥8 and eFI ≥ 0.25 [28, 53, 54]. The choice of frailty tools aims to first, accurately measure frailty in this sample and second, describe the routine usage of different frailty tools across the four nations of the UK [53-59].

Process of care data will be recorded regarding the nature of preoperative assessment, anaesthesia type, catheterisation and postoperative care level.

Multimorbidity is assessed through a list of relevant comorbidities which has been derived from the Charlson Comorbidity Index and a priori knowledge of comorbidities relevant to older patients with frailty and at risk of delirium [60]. The Elixhauser comorbidity index will be calculated from HES data (or equivalent) following the method of Pritchard et al including a one-year look back [61].

Participants who remain inpatients on days three and seven will be assessed for postoperative morbidity using an appropriate speciality specific POMS and either the 4AT (if not critically ill) or CAM-ICU (if critically ill) [45-48, 62]. Delirium and postoperative morbidity will be assumed absent for those discharged alive on the day of surgery.

Those admitted for one or more nights will have a retrospective notes review to identify delirium with the aim of minimising false negatives from researcher assessments alone. This will include medical and nursing documentation, from the day of surgery, up to discharge or day seven postoperatively, whichever is sooner. A tool has been developed to enable objective researcher led retrospective notes evaluation. The tool was developed using DSM-5 criteria for a diagnosis of delirium based on literature review and a priori knowledge of language used by clinicians to describe delirium [63-68]. . Each diagnostic criterion from DSM-5 has been mapped to a set of words and phrases which are commonly used to describe that specific clinical feature.

We aim to minimise the number of missed delirium episodes by combining the findings of the notes review and POMS with either the 4AT or CAM-ICU. This pragmatic approach to the identification of delirium is proposed due to the inherent difficulty in measuring a fluctuating condition with limited resource.

Quality of life will be assessed via email or telephone follow up at 120 days after surgery. The mode of follow up is determined by the participant or their representative. If a participant or their representative has opted into both email and telephone follow up but does not respond to email, the local investigator will be emailed to prompt a telephone call. The EQ-5D-5L and EQ-VAS are validated tools that do not require specific training for accurate use [69]. We will also determine the 'days at home' (DAH) and 'days alive and out of hospital' (DAOH) at 120 days as a measure of the process of recovery that has been shown to be of importance to patients [70]. Days alive and out of hospital is available from central records, and hence easier to collect at scale, but excludes time in residential or nursing home care, outcomes which are often feared by older patients. Days at home, is more difficult to capture, but more closely aligns with what patients want from a good recovery. A possible by product of the study is a demonstration of whether the collection of DAH is worth the additional research burden.

Data linkage via national government held and hospital level datasets will enable us to provide more detailed outcome data without further patient or Local Investigator burden. We will collaborate with NHS Digital, Digital Health and Care Wales, Electronic Data Research and Innovation Service, National Services Scotland and individual Northern Irish hospitals to provide as much of the long-term outcome data as possible. Due to individual countries differing legislation and record keeping, data obtained will vary across the devolved nations.

Data collection for the clinician surveys

The organisational survey, S2 will be distributed via email with a direct link to the REDCap data entry portal. S3 will be administered by researchers (anaesthetists, physicians or research nurses), who will contact medical registrars at the end of an on-call shift. This may be done over the telephone or face to face. The researcher will input their answers directly into REDCap. There will be no ongoing follow up of clinicians.

Analysis plan

Study Cohort:

Descriptive statistics will be used to describe the basic demographics of our participants and key features of our participating sites.

Missing Data:

As with any large study with multiple follow up surveys, there will be missing data. The number and proportion of missing observations will be documented in each analysis. For each variable, we will assess the likely process that led to missing data, to determine whether the data are missing at random or not missing at random. This will determine the choice of an appropriate method of dealing with missing data, for example multiple imputation.

Analysis per objective:

Objective 1: Estimating the incidences of frailty, multimorbidity and postoperative delirium

We will estimate the incidences of our three target variables as the proportion of patients living with frailty and /or multimorbidity, and who experience delirium, respectively. We will

calculate 95 % confidence intervals using the binomial distribution. We will conduct sensitivity analyses with inverse probability weights for elective and emergency procedures in order to account for the absence of weekend data. We have already obtained estimates of the number of emergency and selective procedures carried out at weekends from selected hospitals, and will use those to estimate the inverse probability weights.

Objective 2 & 3: Bivariate analyses

The relationships between frailty, multimorbidity, delirium, primary and secondary outcomes will be reported with appropriate models chosen for different outcome types: multilevel logistic quantile or linear regression. We will account for clustering of patients in hospitals through a random effect for hospitals within mixed-effects models.

Objective 4: Multilevel regression models

To investigate the relationships between frailty, multimorbidity, delirium and a range of outcomes, we will use multilevel regression models adjusting for other clinically relevant preoperative patient characteristics and type of surgery, with hospital-level random intercepts to control for potential between-hospital differences in outcomes. Appropriate models will be chosen for different outcome types: multilevel logistic regression for binary outcomes, multilevel quantile regression for length of stay, DAOH and DAH, and multilevel linear regression for the EQ-5D utility index. Prior to conducting these analyses, we will draw directed acyclic graphs to clarify hypothesized causal relationships and to inform choices of potential covariates that should be included, or indeed excluded, from our models.

Objective 5: Agreement between frailty tools

The analyses for objectives 1-3 will be reported separately for the different frailty measures to gauge differences in their performance as predictors of outcome, using a range of measures of performance as appropriate for the measurement levels of the various outcomes [71]. We won't do the same for the multivariable analyses specified to address objective 4. We will measure the pairwise consistency between the three frailty measures using Spearman's correlation coefficients. To gauge agreement of clinical judgement in practice, we will also assess agreement between dichotomized versions of the three frailty measures, using their respective conventional cut-offs. Agreement between dichotomized frailty measures will be assessed via percentage agreement and kappa coefficient.

Objective 6: Descriptive statistics of interventions

To address the objectives relating to hospital-level and patient-level interventions and perioperative care designed to address risks associated with patient frailty, we will study the sample of patients identified as living with frailty preoperatively and compare them to those identified as not frail. We will document between-hospital differences in interventions and procedures, using descriptive statistics and graphical methods.

Objective 7: Risk prediction model for delirium

Development and internal validation of a risk prediction model for delirium will involve the following steps: (1) Exploratory and graphical analysis of the shapes of the relationships between (numeric) candidate predictors, identified from previous studies and clinical insight, and the probability of delirium. (2) Use of fractional polynomials or splines to identify suitable transformations of numeric predictors, as appropriate. (3) Penalized logistic regression will

be considered for predictor selection, since these have been shown to outperform maximum likelihood estimation and backward selection procedures in the development of risk models [72]. (4) The discrimination of the risk model will be assessed using the C-statistic (area under the ROC curve), which is to be estimated using optimism correction via bootstrapping [73]. We will also calculate the Brier score and investigate model calibration, using graphical displays and the Hosmer-Lemeshow goodness-of-fit statistic. We will follow the TRIPOD statement in reporting the development and internal validation of the risk prediction model for delirium [74].

Objective 8: Descriptive statistics of hospital level models of perioperative care

The national provision of hospital level perioperative medicine services will be described. The description will be sub-divided into care for elective and emergency patients; and degree of preoperative and postoperative services.

Objective 9: Associations between in-depth perioperative interventions and outcomes

The role of in-depth perioperative interventions in modifying the risk of adverse outcomes in patients with frailty will then be assessed using appropriate mixed effects models as for objective 4. Patient-level covariates, such as age, socioeconomic status etc. will be included as appropriate to distinguish the influence of population characteristics with hospital-level perioperative interventions. Although there is inevitably a risk of significant unmeasured confounding it is difficult to estimate the direction or magnitude of these effects.

Objective 10: Acute referrals to medicine from older surgical patients

Descriptive statistics will be used to describe the number and nature of acute referrals to medicine from older surgical patients, and the rate of such referrals by size of hospital (determined by number of beds). The nature of the referrals will be reported as resulting in a telephone or face to face consultation. Referrals will be categorised by surgical speciality, urgency of surgery and primary medical problem.

Objective 11: Identify associations between perioperative medicine services and acute referrals of older surgical patients to medicine

To describe the associations between perioperative medicine services and acute referrals of older surgical patients to medicine, we will use mixed effects logistic regression. Patient level covariates will be included as appropriate to distinguish the relevant perioperative services. Emergency surgery patients will not benefit from an elective perioperative medicine service and so will be analysed separately.

Subgroup analyses:

Data will be reported according to pre-specified subgroups for objectives 1-6. Exact details of subgroups will be finalised once the numbers of patients in potential groups is known. At a minimum the following groups will be reported:

- Emergency and elective procedures
- Surgical invasiveness (using the method described by Abbot et al. [75])
- Major surgical specialty (e.g. orthopaedics, gynaecology)
- The 10 most common healthcare resource groups

Relevant subgroups will be analysed if they include at least 500 participants

Additional analyses and data sharing:
Investigators from outside the core study team may wish to conduct secondary analysis of the data from SNAP 3. We recognise the importance of sharing data within the ethical and legal constraints of the original participants' consent, in order to maximise the potential of our dataset. Following a formal request for data sharing, the request will be considered by the SNAP 3 Study Management Group (SMG) and Steering Committee. If the request is made after the relevant groups have been disbanded, then the request will go directly to the Chief Investigator who will consider the request alongside the Executive Management Board of the HSRC.

There are many potential further analyses possible from the SNAP 3 dataset. We anticipate developing and validating a multimorbidity score for our population. This will then be compared with other measures of multimorbidity to evaluate its ability to predict primary and secondary outcomes. Our secondary analysis plans will continue to evolve as we understand the potential of our cohort's data.

Sample size calculation

Prior to the SARS-CoV-2 pandemic, the estimated achievable sample size for the observational cohort study was around 12,000 participants based on English national data (HES) and previous SNAP projects. We verified that this is a sufficient sample size to achieve the primary and secondary objectives of this study. This estimate has been reduced to 8,000, in light of the impact of the pandemic on health services.

To estimate the proportion of patients living with frailty, and the proportion of patients who develop delirium, a sample size of 7,203 is needed for a margin of error of 1 percentage point (width of 95 % confidence interval: 2 percentage points). This calculation is based on an outcome proportion of 0.25, which is a plausible conservative upper bound. The true proportions are likely to be smaller, which would yield greater precision of the estimation of the true proportion.

To estimate required sample sizes for the delirium risk prediction model, we followed methods published by Riley et al [76]. We made the following assumptions:

- The number of candidate parameters in the risk prediction model is at most 30
- The proportion of patients with delirium is at least 0.05, and at most 0.25
- The Cox-Snell R-square of the prediction model is at least 0.05

These are conservative assumptions. Using the most conservative assumptions in each calculation, the required sample sizes for the following desirable quality criteria are:

- Mean absolute error of predicted probabilities <= 0.01: n = 11,077
- Shrinkage during model development using penalized regression methods <= 5 %: n = 5,395
- Overoptimism of model performance <= 1 %: n = 8,909

These are strict quality criteria, and they suggest that a sample size of around 11,000 patients is sufficient to estimate a high-quality clinical prediction model for delirium.

To achieve the objectives relating to hospital variation in, and effects of, processes and procedures for treating patients with frailty, we plan to estimate multivariate mixed effects

models. There is no precise method for sample size calculations for these kinds of analyses. A conservative lower bound of the percentage of patients with frailty in our achieved sample is 10 %, which implies a minimum sample size of 1,200 patients with frailty. This will give these analyses meaningful precision even in the presence of many covariates.

A priori subgroup analyses will be defined in the statistical analysis plan that will be published separately before data-lock.

ETHICS AND DISSEMINATION

The study has received the following approvals: Scotland A Research Ethics Committee and Wales Research Ethics Committee 7. Ethical approvals are obtained at national level. Local confirmation of capacity and capability is provided by individual hospitals before study commencement.

Patient Consent

All patients who are eligible for SNAP 3 inclusion will have capacity to consent assessed. Those who have capacity to consent to study participation will provide electronic or written consent after being provided with the Participant Information Sheet.

It is essential to include participants without capacity to consent to study participation in order to minimise sampling bias due to exclusion of the target population. The objectives of SNAP 3 relate directly to patients who have both acute and chronic cognitive impairment. This study is of low participant burden and the new knowledge generated will improve care for those without capacity. We will use the process of consultees (in England, Northern Ireland and Wales) and Personal Legal Representatives (PLR, in Scotland) giving advice or consent respectively.

Patient participants who lose capacity to consent:
We anticipate that a proportion of participants will lose capacity to consent during the study, most commonly due to delirium. Whilst it is vital to continue including these participants to fulfil our research objectives, their continued inclusion is complex, and procedures vary depending on the country.

England and Wales:
Those who lose capacity to consent will be treated in accordance with section 34 of the Mental Capacity Act (2005). Information gathered about the participant before loss of capacity will continue to be used in the study. If further interventions are required, then advice will be sought from a consultee for them to continue in the study.

Northern Ireland and Scotland:
Those who lose capacity to consent in Northern Ireland will be treated in accordance with section 132 of the Mental Capacity Act (NI 2016). In the event that a previously consenting participant loses capacity, their statement will still stand unless subsequently withdrawn. In Scotland there is no specific legal provision for those who develop incapacity during research studies. It is generally accepted practice to inform those consenting that they will continue to be included in the study even if they develop incapacity.

Regardless of capacity, if a participant is distressed by ongoing inclusion in the study then they will be withdrawn from the study.

Study management

The SMG is chaired by the Chief Investigator and meets at least monthly, to direct day to day running of the project. The SMG members include those with clinical roles in anaesthesia and geriatrics, a statistician, research management and PPI members. The Study Steering Committee (SSC) meets at least annually to supervise the conduct of the research and its progress achieving the study's objectives whilst working to the protocol. We are fortunate to have multidisciplinary input from all interested clinical groups and lay representation. We are responsible to the HSRC Executive Management Board. The study sponsor is the University of Nottingham.

Patients and public involvement

The topic for SNAP 3 was selected through a competitive process of submissions open to all anaesthetists across the UK. The panel for project selection included representatives from patient and public involvement (PPI) groups, Royal College of Anaesthetists staff, clinicians and trainees.

Our PPI members have provided valuable input into the design and conduct of the study via the SMG and the SSC. They have been influential in the selection of outcome measures especially relating to quality of life. Our PPI members have directly contributed to the format and wording of the patient facing documentation and communication with sites. They have also provided guidance on the acceptability of our study design in relation to participant burden. PPI members will be involved in the publication of our results through our dissemination plans and the production of future public facing documents.

Dissemination

We intend to present the results via our website (hosted by the HSRC), in peer reviewed journals and through conference presentations. We will provide relevant summary reports for the following groups:

1. Our participants- participants will be offered the opportunity to receive summary findings up to three years after recruitment.
2. Our recruiting sites- all sites can receive an overall summary and can request a hospital specific summary.
3. Healthcare policy makers- this will include medical and nursing royal colleges, specialist societies, Department of Health, NHS England, NHS Wales, NHS Scotland and Health and Social Care Ireland.
4. The public- relevant patient groups and charities will be informed of our results with the assistance of our PPI members.
5. Participating NHS Trusts and Health Boards- all NHS Chief Executives will receive a summary of the key findings.

All collaborators who recruit or collect data from participants, or complete clinician surveys will be acknowledged in the manuscripts that arise from this study. Full details can be obtained on our website.

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We would like to acknowledge the hard work and enthusiasm of all of our Local Investigators, Trainee Principal Investigators, Principal Investigators, and the wider SNAP 3 Project Team. We are grateful to the Research and Audit Federation of Anaesthetic Trainees and their local networks for their support of the study.

CONTRIBUTOR STATEMENT

IM initiated the collaborative project; is guarantor; the grant holder; revised the draft paper; cowrote the analysis plan and is analysing the data. CS obtained ethical approval; implemented the study in the UK; designed the data collection tools; monitored data collection for the study; cowrote the statistical analysis plan; cleaned and is analysing the data; and drafted and revised the paper. PM provided statistical expertise in study design and cowrote the analysis plan. JP provided expertise in geriatric medicine; designed data collection tools and revised the draft paper. TP implemented the study in Australia; designed data collection tools and revised the draft paper.

COMPETING INTERESTS

The authors declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

COLLABORATORS: SNAP 3 Project Team: Laura Cortes, Bob Evans, Carol Green, Jose Lourtie, Akshay Shah, Christine Taylor, Karen Williams

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DATA STATEMENT

The data from the SNAP 3 study will be published in a data repository.

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Appendix 1: SNAP 3 Examples of Included and Excluded Procedures

This list contains examples of included and excluded procedures for SNAP 3. We hope that it will be useful when making decisions regarding whether a participant should be approached for the study. It is not designed to be comprehensive, most surgical procedures are included. We have tried to not include the very minor procedures but it is challenging to know where to draw the line. We hope this guidance is useful.

Ophthalmology

Include	**Exclude**
Corneal grafts	Any procedure under topical anaesthesia
Scleral buckle	LASER (cornea, medical retina)
Eyelid reconstruction	Adnexal (eyelid surgery inc. ptosis, blepharoplasty)
Keratoplasty	Removal of oil from vitreous body
Excision of scalp/skin lesions **if require a split skin graft (SSG) or flap**	Excision of scalp/skin lesions **not requiring a SSG or flap**
Vitreoretinal surgery	Superficial eye lid surgery
Strabismus surgery	Vitrectomy using pars plana approach
Enucleation/eviscerations/orbital decompression	Correction of entropion of lower eyelid
Radioactive plaque insertion & removal	Dacryocystorhinostomy
Tantalum markers	Cataract surgery
Glaucoma surgery	Removal of sutures
Anterior orbitotomy	Needling
Trabeculectomy	Preserflo microshunt & mitomycin-C
Retinal surgery anaesthesia	Cataract surgery (regardless of anaesthesia mode)

General Surgery

Include	**Exclude**
Inguinal hernia repair under local anaesthesia +/- sedation	Lymph node biopsy
VAC dressing change	Simple dressing change
Perianal excision of rectal polyp	Diagnostic and therapeutic endoscopy regardless of anaesthesia mode
EUA rectum	
Manual evacuation	
Axillary clearance	
Oesophageal dilation/stenting	

ENT

Include	Exclude
Excision of larger lesions e.g basal cell carcinoma (BCC)/squamous cell carcinoma (SCC) **e.g. requiring more than primary closure, SSG/flap.** NB. Mode of anaesthetic here does not influence decision	Excision of smaller BCC/SCC **e.g. no SSG/flap required.** NB. Mode of anaesthetic here does not influence decision
Microlaryngoscopy	Biopsy of tongue
Minimally invasive parathyroidectomy	Frenuloplasty
Manipulation or examination under anaesthetic nose	Removal salivary tube
Cervical lymph node biopsy if GA	Tracheostomy insertion/change
Panendoscopy	Grommets
	Anaesthesia for diagnostic procedures
	Tracheo-oesophageal puncture
	Thyroplasties
	Tracheostomy insertion/change

Thoracics

Include	Exclude
Diagnostic bronchoscopy if with other procedure	Endobronchial ultrasound (EBUS)
Tracheal stenting	Diagnostic bronchoscopy alone
Rigid bronchoscopy	Diagnostic and therapeutic bronchoscopy/pleuroscopy
Mediastinoscopy	Chest drain as sole procedure
Video assisted thoracoscopic surgery (VATS)	
Endoscopic procedures performed ancillary to surgical procedure ○ Bronchoscopy prior to lung resection	

Cardiac

Include	Exclude
Transcatheter aortic valve implantation (TAVI)	Ablations
Other minimally invasive valve replacement procedures carried out under general anaesthesia	PPM lead extractions
	Angiography, percutaneous coronary intervention (PCI)

	Insertion of permanent pacemaker (PPM) / implantable cardioverter defibrillator (ICD)
	Cardioversion
	Electrophysiology (diagnostic or therapeutic)
	Insertion of intra-aortic balloon pump (IABP)

Hands

Include	**Exclude**
	Carpal tunnel decompression under local anaesthetic
	Dupuytren's palmar fasciectomy
	Trigger finger release
	Excision of hand lesion if small

Trauma & Orthopaedics Emergency Department

Include	**Exclude**
Ulnar nerve transposition	Aspiration of knee under local anaesthetic
Removal of metal work	Cheilectomy
Excision of olecranon bursa	Trigger point injections
Vertebroplasty	Therapeutic epidural injection
Trapeziectomy	Intra-articular joint injections
Knee replacement	Dupuytren's fasciectomy
Osteotomy of any bone	MUA joint
Replacement of hip joint	MUA fracture in ED
Replacement of shoulder joint	General anaesthesia/sedation for scanning/ICU management only
Small joint fusion	Post-arrest management
Insertion K wire	Erector spinae catheters
MUA fracture in theatre	Joint injections
Surgery for trauma	Joint aspiration
MUA fractures/dislocations in theatre	
Joint washout	

Urology

Include	**Exclude**
Rigid cystoscopy	Flexible cystoscopy
Urethral dilatation	Circumcision under local anaesthetic
Transurethral resection of bladder tumour	Standard circumcision under general anaesthetic
Transurethral resection of prostate	Transperineal prostate biopsy

Hydrocele under general anaesthetic	Flexible ureteroscopy
Laser fragmentation of stone	Cystoscopy under local anaesthesia
Nephrostomy	Prostate brachytherapy
TURP/TURBT	
Rigid diagnostic/surveillance cystoscopy	
Stent change	

Vascular

Include	**Exclude**
Fistula ligation and banding	Varicose veins under local anaesthetic
Fistula creation	
Endovascular aneurysm repair (EVAR)	

Interventional Radiology

Include	**Exclude**
EVAR	CT guided biopsies
Angioplasty	IV access/line insertion
CT guided drain	Endoscopic retrograde cholangiopancreatography (ERCP)

Dental

Include	**Exclude**
Extractions	

Gynaecology

Include	**Exclude**
Therapeutic hysteroscopy	**Diagnostic** hysteroscopy +/- biopsy
Laparoscopic hysterectomy	Hysteroscopy and smear
Cervical polypectomy	

Neurosurgery

Include	**Exclude**
Sympathetic nerve stimulator insertion or removal	SNS battery or lead change
Spinal cord stimulator insertion	SNS reprogramming
	SCS trial if purely percutaneous

Appendix 2: SNAP 3 Case Report Form

Below are the questions used in REDCap for the SNAP 3 study. For brevity, previously published, validated tools have not been replicated in this document. References for tools used in the SNAP 3 study can be found in the reference list of our accompanying paper.

1.0	**Participant details**				
1.1	Which country is your hospital based in?	England	Northern Ireland	Scotland	Wales
1.2	Which hospital site are you completing this form for?				
1.3	Is the potential participant having surgery AND 60 years or above?	Yes		No	
1.4	What is the planned date of surgery?				
1.5	Does the potential participant have the capacity to consent?				
1.6	Is there a consultee/Personal Legal Representative (PLR) to offer advice? This may be face to face or over the telephone.	Yes		No	
1.7	Is the participant's Consultee (England, Wales and Northern Ireland) or Personal Legal Representative (Scotland) available in person or over the telephone?	Yes		No	
1.8	Participant first name				
1.9	Participant surname				
1.10	Participant date of birth				
1.11	Participant NHS/CHI/H&C number				
1.12	Would the participant/Consultee/PLR be able to complete a survey at 4 months by email or telephone?	Yes by email	Yes by telephone	No	
1.13	Email address				
1.14	Telephone number				

2.0	**Frailty assessment**				
2.1	At any point during the participant's clinical pathway, were they assessed for frailty?	Yes		No	
2.2	Which frailty tool was used to assess the participant?	Clinical Frailty Scale /Rockwood Frailty Scale	Edmonton Frailty Scale (scored out of 17)	Reported Edmonton Frail Scale (scored out of 18)	Groningen Frailty Indicator
		Gait Speed Test	PRISMA-7	Risk Analysis Index-C	Timed Up and Go (TUG) Test
		Electronic Frailty Index	Hospital Risk Frailty Index	Grip Strength	Comprehensive Geriatric Assessment
2.3	What was the result of the frailty tool?				
2.4	Clinical Frail Scale (as completed by the clinical or research team)	1-9			
2.5	Reported Edmonton Frail Scale (as completed by the clinical or research team)	0-18			
2.6	Electronic frailty index	0-36			
3.0	**Demographics and ADLs**				
3.1	Postcode				
3.2	Ethnic group	Census categories			
3.3	Highest level of education	Degree level eg. degree, NVQ Level 4-5, Higher National Certificate, Higher National Diploma, BTEC Higher Level, professional	2+ A levels/VCEs, 4+ AS Levels, Higher School Certificate, NVQ Level 3, Advanced GNVQ, City and Guilds Advanced Craft, BTEC National, Scottish Higher	Apprenticeship	5 or more O Levels (passes)/CSEs (grade 1), School Certificate, 1 A Level, 2-3 AS Levels/VCEs, NVQ Level 2, Intermediate GNVQ, City and Guilds Craft, BTEC, Scottish Higher,

		qualifications (eg. teaching or nursing) or other equivalent higher education qualifications	National Diploma, Scottish Higher National Certificate, SVQ level 4+) or equivalent		Scottish Advanced Higher or equivalent qualifications
		O levels/CSEs (any grade), Foundation Diploma, NVQ level 1, Foundation GNVQ, O grade, Scottish Standard Grade or equivalent qualifications	No formal qualifications	Don't know	
3.4	Biological sex	Female		Male	
3.5	Weight				
3.6	Height				
3.7	BMI				
3.8	Source of admission	Own home	Sheltered housing, retirement complex	Residential home	Nursing home
		Rehabilitation facility (inpatient community unit or care home with the purpose of short term rehabilitation)	Homeless	Another secondary care hospital	Other, please specify

3.9	Help with activities of daily living (ADLs)	No, the participant receives no help with ADLs or the participant has help for lifestyle reasons only (would easily be able to do the tasks if needed).	Needs help with any of the following: transportation, shopping, managing finances, shopping, meal preparation, house cleaning, managing communication with others, managing medications.	Needs help with any of the following: ambulating, feeding, dressing, personal hygiene, continence, toileting.	
4.0	**Preoperative assessment**				
4.1	How was the participant assessed preoperatively?	Nurse (or AHP) led assessment on day of surgery only	Anaesthetist led assessment on day of surgery only	Nurse (or AHP) led clinic	Anaesthetist led clinic
		Physician (non geriatrician) led clinic	Geriatrician led clinic	MDT clinic	Other
		None of the above			
4.2	Urgency of surgery as per NCEPOD criteria	Emergency	Urgent	Expedited	Planned
4.3	Indication for surgery	Confirmed cancer	Possible cancer e.g. surgery with the aim of diagnosing possible cancer	Non-cancer	
4.4		ASA I	ASA II	ASA III	ASA IV

	Which ASA score would you give the participant?	ASA V			
4.5	Surgical Outcome Risk Tool (SORT) Version 2 (including procedure type and surgical speciality, as completed by the clinical or research team)				
5.0	**Comorbidities**				
5.1	Does the participant have any of the following comorbidities?	MI (history of MI based on patient history, notes, history of stent	Heart failure (dyspnoea that has responded to heart failure treatment)	AF (paroxysmal/permanent AF, not if successfully ablated)	Valvular heart disease
		Hypertension (even if treated, do not include those with one isolated episode)	Peripheral vascular disease (treated and untreated)	COPD (probable clinical diagnosis)	Other chronic lung disease
		OSA/obesity hypoventilation syndrome (symptomatic, not purely positive STOP-BANG)	Cerebrovascular disease with mild or no residual symptoms (includes TIA, intracerebral/subarachnoid haemorrhage and stroke diagnosed on CT with no symptoms)	Hemiplegia or paraplegia (from any cause)	Dementia
		Mild cognitive	Anxiety or depression	Parkinson's disease	Diabetes (not just

		impairment	(on treatment)	or parkinsonism	impaired glucose tolerance or if in remission)
		Moderate or severe renal disease (acute or chronic, stage 3A+, eGFR< 60)	Benign prostatic hypertrophy (can be self reported)	Liver disease (with or without portal hypertension)	Peptic ulcer disease (even if treated and not symptomatic)
		Malignancy	Lymphoma (of any type, acute or chronic)	Leukaemia (of any type, acute or chronic)	Connective tissue/rheumatological disease (systemic lupus erythematosus, polymyositis, mixed connective tissue disease, polymyalgia rheumatica, psoriatic arthropathy or rheumatoid arthritis)

		Osteoarthritis (include self reported)	AIDS	Hearing impairment (uses hearing aids or struggles to manage a conversation at usual volumes of speech)	Visual impairment (registered partially sighted)
5.2	Does the participant have complications from their diabetes?	Diabetes without chronic complication		Diabetes with chronic complication	
5.3	How severe is the participant's liver disease?	Mild liver disease (without portal hypertension)		Moderate or severe liver disease (with portal hypertension)	
5.4	Which type(s) of malignancy does the participant have/has had?	Any solid malignancy without metastases		Metastatic solid tumour	
5.5	When was participant's malignancy/malignancies first diagnosed?	≤ 5 years ago		> 5 years ago	
6.0	Investigations within 12 weeks				
6.1	Haemoglobin g/L				
6.2	White cell count 10^9/L				
6.3	Neutrophil 10^9/L				
6.4	Lymphocyte 10^9/L				
6.5	Sodium mmol/L				
6.6	Potassium mmol/L				
6.7	Creatinine micromol/L				
6.8	eGFR ml/min/1.73^2				

6.9	What is the participant's SARS-Cov-2 status preoperatively?	Tested positive or not tested and treated as positive	Tested negative or not tested and treated as negative	Don't know	
7.0	Day of procedure				
7.1	Date of operation				
7.2	Type of anaesthesia	General anaesthesia with volatiles	General anaesthesia with total intravenous anaesthesia (TIVA)	Neuraxial	Regional
		Sedation	Local infiltration	Don't know	
7.3	Was the participant catheterised?	No	Long-term/pre-admission catheter	Electively catheterised pre/intra-op	Catheterised post-op
7.4	What level of care did the participant receive postoperatively (on the day of surgery)?	Ward (level 0 or 1 care, including day case units)	Unplanned admission to PACU or equivalent (level 1.5 care)	Unplanned admission to PACU or equivalent (level 2/3 care)	Unplanned critical care admission (level 2 or 3 care)
		Planned admission to PACU or equivalent (level 1.5 care)	Planned admission to PACU or equivalent (level 2/3 care)	Planned critical care admission (level 2 or 3 care)	Don't know
7.5	Was the participant a day case patient who has been successfully discharged?	Yes, they have been discharged on the day of surgery	No, they are planned to be an inpatient OR they were intended to be day case but haven't been	Don't know	

			discharged on the day of surgery		
8.0	Day 3 follow up				
8.1	Postoperative Morbidity Survey (general/cardiac/fractured neck of femur, as completed by the research team)				
8.2	Documented new confusion or delirium	Yes		No	
8.3	4AT (if the participant isn't critically unwell, as completed by the clinical or research team)	0-12			
8.4	CAM-ICU (if the participant is critically unwell, as completed by the clinical or research team)	Negative		Positive	
8.5	Does the participant recall any symptoms of postoperative delirium or 'acute confusion'?	Yes		No	
9.0	Day 7 follow up				
9.1	Postoperative Morbidity Survey (general/cardiac/fractured neck of femur, as completed by the research team)				
9.2	Documented new confusion or delirium	Yes		No	
9.3	4AT (if the participant isn't critically unwell, as completed by the clinical or research team)	0-12			
9.4	CAM-ICU (if the participant is critically unwell, as completed by the clinical or research team)	Negative		Positive	
9.5	Does the participant recall any symptoms of	Yes		No	

	postoperative delirium or 'acute confusion'?				
10.0	Delirium notes review				
	SNAP 3 will use the validated 4AT and CAM-ICU to detect delirium in participants postoperatively. Due to its fluctuating nature, some participants will not be experiencing delirium at the time of their follow up even though they have had delirium. We would like to maximise the likelihood of detecting delirium by undertaking a notes review on day seven in addition to the validated assessment tools. The notes review will provide the study with an impression of whether or not a patient experienced delirium outside of the time of their delirium assessment. Based on existing literature, a notes review is more likely to detect delirium which occurs at night and hyperactive delirium, than a single assessment (such as CAM) alone. The diagnosis of delirium is often not clearly documented in patient's notes. Estimates of previously unrecognised delirium from retrospective notes are variable, ranging from 7-43%. Nursing notes are more likely than medical notes to document the presence of keywords indicating delirium. The use of DSM-V criteria expanded with words describing delirium have been selected based on previous literature and a priori knowledge. Please review the nursing and medical notes as below. Only record evidence from (up to and including) day seven postoperatively. If there is evidence of delirium occurring on day eight, then please do not report this. If you believe that you have identified a current diagnosis of unrecognised delirium from the notes then please pass these concerns to the clinical team. This is a requirement of good clinical and research practice.				
10.1	If the participant has a diagnosis of delirium documented either using a validated tool or as free text documentation of 'delirium' or 'delirious', then please select 'Positive diagnosis of delirium'	Positive diagnosis of delirium	No explicit diagnosis of delirium	Don't know	
	The following questions summarise the DSM-V criteria for the diagnosis of delirium and give examples of words frequently used to describe delirium in the clinical notes.				
10.2	DSM criteria A: Is there any documentation of the following? Inattention, inattentive, distractable Muddled Drowsy, drowsiness	Yes, phrases similar to the ones listed are used in the notes	No	Don't know	

	Unrousable, unresponsive Hypoactive Agitated, agitation Altered mental status Inability to count from 20-1 Inability to recite months of the year backwards				
10.3	DSM criteria B: Is there any documentation of the following? Acute confusion Fluctuating confusion Fluctuation in severity throughout the day Altered mental status, mental status change	Yes, phrases similar to the ones listed are used in the notes	No	Don't know	
10.4	DSM criteria C: Is there any documentation of the following? Confused, confusion Muddled Hallucination, hallucinating Reorientation, reorientated Disorientation, disorientated, Encephalopathy, encephalopathic, Agitated, agitation Inappropriate behaviour Restless, unsettled Aggressive Wandering Refusing observations/ interventions Uncooperative, not cooperating, Pulling lines out Combative Speaking nonsense Paranoid MoCA < 24 AMTS < 7	Yes, phrases similar to the ones listed are used in the notes	No	Don't know	

10.5	DSM criteria D1: Is the participant functioning at their cognitive baseline?	Yes (they are at their neurocognitive baseline according to available sources of evidence)	No	Don't know	
10.6	DSM criteria D2: If delirium is likely, could this disturbance be better explained by a severely reduced level of arousal or coma? *If suffering from delirium, are the participant's symptoms better explained by being severely obtunded, sedated or unconscious with a Richmond Agitation Sedation Scale of 4 or less?*	Yes	No	Delirium not likely	
	Positive diagnosis of delirium from notes review either from:	Documented diagnosis of delirium in notes	DSM criteria responses: Yes to 10.2, 10.3, 10.4 No to 10.5, 10.6		
11.0	4 month follow up				
11.1	EQ-5D-5L				
11.2	EQ-VAS	0-100			
11.3	From when you had your operation, until 120 days after surgery, how many days have you spent in any hospital? Please include any hospital admissions (including your initial admission for surgery) and rehabilitation in hospitals. If you have				

	been out of hospital since the day of surgery and the surgery was day case then write '0'	
11.4	From when you had your operation, until 120 days after surgery, how many days have you spent from home due to convalescing with family/friends/in residential homes. Don't include days spent socialising away from home or hospital admissions here. If you have been at home since the day of surgery and the surgery was day case then write '0'	

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page/Line	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1/L4-6	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2/L10-18	Protocol paper so no results available
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4/L3-P5/L37	
Objectives	3	State specific objectives, including any prespecified hypotheses	P5/L39-P6/L24	
Methods				
Study design	4	Present key elements of study design early in the paper	P6/L26	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P6/L27-P7/L15-37, P8/L39-47	
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P8/L6-L37, P10/L2-22	
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P7/L17-P8/4, P9/L8-P10/L14, see also Appendix 2	Also see CRF appendix
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P9/L8-P10/L22	
Bias	9	Describe any efforts to address potential sources of bias	P3/L6, P3/L13-16, P9/L34-47, P10/L2-5	
Study size	10	Explain how the study size was arrived at	P13/L17-P14-L4	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P9/L15-16, P9/L23-47	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to	P10/L31-	

		control for confounding	P13/L15	
		(*b*) Describe any methods used to examine subgroups and interactions	P12/L38-46	
		(*c*) Explain how missing data were addressed	P10/L36-42	
		(*d*) If applicable, explain how loss to follow-up was addressed	Protocol paper so not possible	
		(*e*) Describe any sensitivity analyses	P11/L1-5	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Protocol paper so not possible.	
		(b) Give reasons for non-participation at each stage	Protocol paper so not possible.	
		(c) Consider use of a flow diagram	Protocol paper so not possible.	Protocol paper so not possible.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Protocol paper so not possible.	Protocol paper so not possible.
		(b) Indicate number of participants with missing data for each variable of interest	Protocol paper so not possible.	Protocol paper so not possible.
		(c) Summarise follow-up time (eg, average and total amount)	Protocol paper so not possible.	Protocol paper so not possible.
Outcome data	15*	Report numbers of outcome events or summary measures over time	Protocol paper so not possible.	Protocol paper so not possible.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Protocol paper so not possible.	Protocol paper so not possible.
		(*b*) Report category boundaries when continuous variables were categorized	Protocol paper so not possible.	Protocol paper so not possible.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Protocol paper so	Protocol paper so

			not possible.	not possible.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Protocol paper so not possible.	Protocol paper so not possible.
Discussion				
Key results	18	Summarise key results with reference to study objectives	Protocol paper so not possible.	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P3/L8-16	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Protocol paper so not possible.	Protocol paper so not possible.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Protocol paper so not possible.	Protocol paper so not possible.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P16/L40-44	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.