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Functional Improvement Trajectories After Surgery (FIT After Surgery) study: protocol for a multicentre prospective cohort study to evaluate significant new disability after major surgery in older adults

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ABSTRACT

Introduction Older adults prioritise surviving surgery, but also preservation of their functional status and quality of life. Current approaches to measure postoperative recovery, which focus on death, complications and length of hospitalisation, may miss key relevant domains. We propose that postoperative disability is an important patient-centred outcome to measure intermediate-to-long recovery after major surgery in older adults.

Methods and analysis The Functional Improvement Trajectories After Surgery (FIT After Surgery) study is a multicentre cohort study of 2000 older adults (≥65 years) having major non-cardiac surgery. Its objectives are to characterise the incidence, trajectories, risk factors and impact of new significant disability after non-cardiac surgery. Disability is assessed using WHO Disability Assessment Schedule (WHODAS) 2.0 instrument and participants' level-of-care needs. Disability assessments occur before surgery, and at 1, 3, 6, 9 and 12 months after surgery. The primary outcome is significantly worse WHODAS score or death at 6 months after surgery. Secondary outcomes are (1) significantly worse WHODAS score or death at 1 year after surgery, (2) increased care needs or death at 6 months after surgery and (3) increased care needs or death at 1 year after surgery. We will use multivariable logistic regression models to determine the association of preoperative characteristics and surgery type with outcomes, joint modelling to characterise longitudinal time trends in WHODAS scores over 12 months after surgery, and longitudinal latent class mixture models to identify clusters following similar trajectories of disability.

Ethics and dissemination The FIT After Surgery study has received research ethics board approval at all sites. Recruitment began in December 2019 but was placed on hold in March 2020 because of the COVID-19 pandemic. Recruitment was gradually restarted in October 2020, with 1-year follow-up expected to finish in 2023.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A large generalisable sample of older adults will be used to characterise the incidence, trajectories, risk factors and impact of new postoperative disability.
⇒ Baseline evaluation characterises important prognostic factors, including social supports, comorbidities, frailty, depression, pain and physical performance tests.
⇒ Participants undergo close prospective follow-up to ascertain disability, survival, complications, quality of life, depression, pain and decision regret.
⇒ Limitations include loss to follow-up, selection bias, reliance on self-reported measures of postoperative functional status and impact of the COVID-19 pandemic.

Publication of the primary results is anticipated to occur in 2024.

INTRODUCTION

About 190 million people have major surgery in high-income countries every year.[1] An increasing proportion of these individuals are older adults with concomitant frailty and comorbid disease.[2] Importantly, advanced age, comorbidity burden and frailty are themselves associated with increased morbidity, mortality and health resource utilisation after surgery.[3–6] These trends highlight the need to re-evaluate how patients, clinicians, researchers and administrators characterise optimal recovery after surgery. Typical standard approaches to measure postoperative recovery have focused on routinely measured

events such as death, major complications and length of hospitalisation. Since these outcomes may miss important domains that are especially relevant to older adults,[7] significant postoperative disability has gained increasing attention as a patient-centred postoperative outcome.[8]

Based on the International Classification of Functioning, Disability and Health framework,[9 10] disability is an umbrella term that covers impairments in body function (ie, physiological functions of body systems), limitations in activity (ie, difficulties executing tasks or actions) and participation restrictions (ie, problems with involvement in life situations). Freedom from significant new disability has several advantages as a measure of intermediate-to-long term recovery after major surgery. First, older adults report freedom from disability as being a highly important postoperative outcome.[7] Indeed, they may prioritise preservation of function and cognition over survival when making treatment decisions for life-threatening diseases.[11] Second, disability integrates the overall impact of various adverse events (eg, myocardial infarction, acute stroke, surgical site infection) on patients' recovery after surgery. Third, disability has validity as a measure of postoperative recovery. For example, when compared with individuals with uncomplicated hospital stays after surgery, individuals with serious complications are significantly less likely to return to functional independence by 3–6 months after surgery.[12] Fourth, disability can capture adverse intermediate-to-long term sequelae after a seemingly uncomplicated recovery following surgery. Even in the absence of a major postoperative complication, a recent cohort study found that one in 10 adults reported a decline in function (ie, mobility, self-care, usual activities) at 1 year after major non-cardiac surgery.[13] Finally, there are several valid and feasible options to ascertain disability after surgery. For example, patients might be asked about increased care needs after surgery (eg, discharge home with support services or discharge to a chronic care facility).[14] An international consensus-based panel has also recommended a disability questionnaire, the 12-item WHO Disability Assessment Schedule (WHODAS) version 2.0, for inclusion as a core patient-centred outcome in perioperative studies.[8] The WHODAS is a reliable and valid instrument that is scored within 5 min, available in multiple formats (ie, self-report, proxy, telephone), and translated into several languages.[9 10] The questionnaire has good to excellent acceptability, responsiveness and validity in surgical patients.[15]

While postoperative disability is an important, patient-centred and feasibly measured outcome, there remain limited multicentre data on its incidence, predictors and impact. Such data have the potential to positively impact the perioperative arena. For example, accurate risk estimates will facilitate early identification of patients at elevated risk of postoperative disability, who can then be targeted for interventions in the preoperative (eg, prehabilitation)[16] or postoperative (eg, enhanced hospital discharge plans)[17] period. Since one-third of patients report deficiencies in information required to align their values and preferences with expected outcomes before major surgery,[18] more accurate and patient-centred presentation of possible deleterious postoperative outcomes will also improve the informed consent process and support shared decision-making for surgery.[19–21]

To help better understand the incidence, trajectories, risk factors and impact of new significant disability after major elective non-cardiac surgery in a large generalisable cohort of older adults, we are conducting the Functional Improvement Trajectories After Surgery (FIT After Surgery) study. The main objectives of this multicentre prospective cohort study are presented below.

Primary objective

1. To estimate the risk of significant new disability or death within 1 year following major elective non-cardiac surgery in older adults (≥65 years).

Secondary objectives

1. To characterise the association of preoperative factors and surgery type with significant new disability or death within 1 year after major non-cardiac surgery in older adults.
2. To characterise the different trajectories of disability over 1 year following major non-cardiac surgery in older adults.

METHODS AND ANALYSIS

Study design

The FIT After Surgery study is a prospective cohort study of 2000 older adults having major elective non-cardiac surgery at 16 centres in Canada. The study design is outlined in figure 1.

Participant eligibility criteria

Potential participants are recruited from preoperative assessment clinics, surgeons' clinics or surgical wards at participating sites. Eligible patients are aged 65 years or older and scheduled to have elective non-cardiac surgery with a minimum expected postoperative stay of two nights or longer. The age threshold of 65 years or older for defining older adults is consistent with prior work in geriatric surgery.[22] Elective surgery includes time-sensitive scheduled procedures where delays exceeding 1–6 weeks could negatively affect outcome (eg, curative intent cancer surgery). Exclusion criteria include endovascular surgery, total joint replacement surgery, intracranial neurosurgery, surgery with no curative intent (eg, palliative cancer surgery) and known severe dementia. Severe dementia is defined as dependence in all basic activities of daily living, a Folstein Mini-Mental State Examination score less than 10[23] or stage 6 or 7 on the Reisberg Alzheimer's Scale.[24] All participants provide informed consent at time of recruitment to the study.

Longitudinal assessment of disability

The extent of any disability in study participants is assessed before surgery, and then at 1, 3, 6, 9 and 12 months after

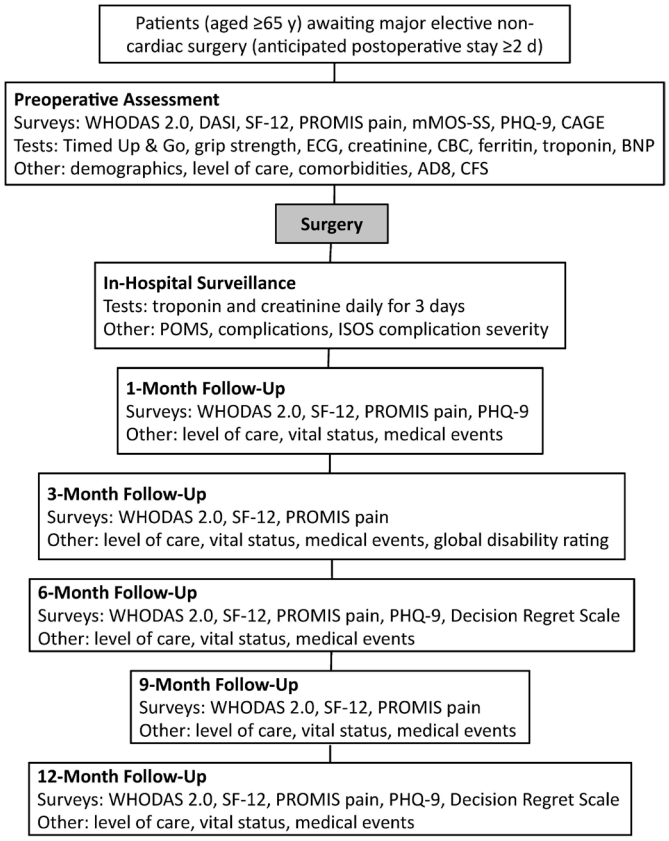

Figure 1 Overall design of the FIT After Surgery cohort study. AD8, Ascertain Dementia 8-item; BNP, brain natriuretic peptide; CBC, complete blood count; CFS, Clinical Frailty Scale; DASI, Duke Activity Status Index; ISOS, International Surgical Outcomes Study; mMOS-SS, modified Medical Outcomes Study Social Support Survey; PHQ-9, Patient Health Questionnaire-9; POMS, Postoperative Morbidity Survey; PROMIS, Patient-Reported Outcomes Measurement Information System; SF-12, Short Form 12; WHODAS, WHO Disability Assessment Schedule.

surgery, using both the 12-item WHODAS 2.0 questionnaire and level-of-care needs. The WHODAS disability score ranges from 0 to 48, which can be expressed as a percentage of the maximum possible score. A WHODAS score of 12 or greater (≥25%) represents moderate or greater restrictions in activities and participation,[10] which is consistent with normative data in the non-operative setting.[25] Recent psychometric evaluation of the WHODAS 2.0 in a sample of adult surgical patients (mean age 67 years, SD 13, range 18–103) found the minimum clinically important difference to be 5%.[26] Level-of-care needs are categorised as (1) living at home without support or skilled services, (2) living at home with support or skilled services and (3) living in a care facility such as a nursing home.[14] The definition of 'home' includes retirement homes without 24-hour nursing care, but not long-term care homes or nursing homes that provide 24-hour nursing and personal care.

Other preoperative baseline assessments

At the time of recruitment, participants' age, sex, ethnicity, educational level, home living situation, comorbidities, recent chemotherapy, smoking status, history of falls in prior 6 months and use of mobility aids are documented (table 1).

In addition, research personnel apply the Clinical Frailty Scale (CFS) to assess for frailty and the Ascertain Dementia 8-item (AD8) interview to screen for dementia.[27 28] Study personnel complete standardised training to ensure consistent application of the CFS.[29] Participants complete other validated questionnaires, namely the Duke Activity Status Index to characterise self-reported cardiorespiratory fitness,[30] the Short Form 12 (SF-12) to characterise health-related quality of life,[31] the Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Intensity Form 1a to assess pain intensity,[32] the PROMIS Pain Interference Short Form 6a to assess the consequences of pain on relevant aspects of a person's life,[32] the Patient Health Questionnaire 9 (PHQ-9) questionnaire to screen for depression,[33] the modified Medical Outcomes Study Social Support Survey (mMOS-SS) questionnaire to measure social supports[34] and the CAGE (Cut, Annoyed, Guilty, and Eye) questionnaire to screen for alcohol use disorder.[35] Participants undergo a baseline ECG and blood tests (complete blood count, creatinine, ferritin, brain natriuretic peptide), in addition to performing two brief physical performance tests according to standardised protocols. The physical tests are the Timed Up and Go test and grip strength assessment using a Jamar hand dynamometer.[36]

Follow-up procedures

On the day of surgery, research personnel document information on surgery type, intraoperative care and postoperative disposition. Participants are then followed daily throughout their hospital stay. While participants remain in hospital, follow-up procedures include administration of the Postoperative Morbidity Survey (POMS)[37] and blood sampling to measure troponin and creatinine concentrations. The POMS instrument is administered on the third and fifth days after surgery. Blood sampling is performed daily for the first 3 days after surgery, with the specific troponin assays being the preferred assays at each study site. Research personnel also document specific complications (table 2), with the most severe complication being further characterised using a modified International Surgical Outcomes Study scheme.[38] In this classification scheme, the most severe complication is classified as mild (resulted in only temporary harm and did not require clinical treatment), moderate (required clinical treatment but without causing significant prolongation of hospital stay or permanent functional limitation), severe (required clinical treatment and resulted in significant prolongation of hospital stay and/or permanent functional limitation) or fatal (resulted in death).

After participants are discharged from hospital, further follow-up is conducted by the central FIT After Surgery project coordination team at the Applied Health Research Centre (Unity Health Toronto, Toronto, Ontario, Canada). During the assessments, which occur at 1, 3, 6,

Table 1 Definitions of preoperative characteristics

Variable	Definition
Highest educational level attained	1. Primary school or less (up to grade 8) 2. Some high school 3. Completed high school 4. Some college/university but did not finish 5. Undergraduate degree/diploma from college/university 6. Graduate school 7. Prefer not to respond
Living situation at home*	1. Not living at home 2. Living at home alone 3. Living at home with spouse or common-law partner (±others) 4. Living at home with other family (excluding spouse or common-law partner) 5. Living at home with non-family members
Use of a gait or mobility aid	Use of a device to improve walking pattern, balance or safety while mobilising independently (eg, canes, crutches or walkers)
Coronary artery disease	History of any of the following: angina, myocardial infarction, positive exercise stress test, positive nuclear or echocardiographic stress testing, wall motion abnormalities on echocardiogram, coronary angiography with evidence of ≥50% vessel stenosis, ECG with pathological Q-waves in two contiguous leads
Recent high-risk coronary artery disease	A physician diagnosis within the 6 months prior to non-cardiac surgery of a myocardial infarction, acute coronary syndrome, Canadian Cardiovascular Society Class III or IV angina[53]
Heart failure	Physician diagnosis of heart failure, chest X-ray showing pulmonary vascular redistribution or oedema
Atrial fibrillation	Defined as any episode within the previous year
Cerebrovascular disease	Physician diagnosis of stroke, imaging (CT or MRI) evidence of previous stroke or history of transient ischaemic attack
Peripheral artery disease	Physician diagnosis of peripheral artery disease, history of ischaemic intermittent claudication or rest pain, history of revascularisation procedure to legs, peripheral arterial obstruction of ≥50% luminal diameter or ankle/arm systolic blood pressure ratio ≤0.90 at rest
Diabetes mellitus	Current diabetes mellitus with further categorisation of therapy required as (1) insulin requiring, (2) non-insulin medications alone and (3) diet control alone
Hypertension	Physician diagnosis of hypertension
Smoking status (pertains to cigarettes or cigars)	1. Current: any smoking within previous 7 days 2. No smoking within previous 7 days, but did otherwise smoke within previous 1 year 3. No smoking in previous 1 year, but did smoke before that 4. No history of smoking
Obstructive pulmonary disease	Physician diagnosis of asthma, reactive airways disease, chronic obstructive lung disease, chronic bronchitis or emphysema
Chronic liver disease	Physician diagnosis of chronic hepatitis or cirrhosis
Known dementia or cognitive impairment	Physician diagnosis of dementia (any aetiology) or chronic cognitive deficit
Physician diagnosis of depression	Physician diagnosis of depression
Current dialysis	Use of a haemodialysis machine or peritoneal dialysis apparatus
Malignancy (for skin cancers, only melanoma should be considered)	1. No history of cancer 2. History of cancer: unrelated to proposed surgery 3. History of cancer: indication for proposed surgery
Metastatic solid tumour (excluding non-melanoma skin cancers)	Any history of a metastatic solid tumour
Preoperative chemotherapy for malignancy	Defined as chemotherapy within 90 days before scheduled surgery
Arthritis (osteoarthritis or inflammatory arthritis)	1. No documented history of arthritis 2. Documented history of arthritis: no joint replacement surgery (previous surgery or currently scheduled surgery) 3. Documented history of arthritis: previous or scheduled joint replacement surgery
Connective tissue disease	Physician diagnosis of systemic lupus erythematous, polymyositis, mixed connective tissue disease, polymyalgia rheumatica, moderate-to-severe rheumatoid arthritis, vasculitis or any other systemic vasculitis
Falls in the preceding 6 months	An unexpected event in which the participants come to rest on the ground, floor or lower level within prior 6 months[54] Classified as: 1. None 2. One fall 3. Two or more falls

*Definition of 'home' includes retirement homes without 24-hour nursing care but excludes long-term care homes or nursing homes that provide 24-hour nursing and personal care.

Table 2 Definitions of postoperative events

Event	Definition
Status at hospital discharge	► Not alive ► Alive to home without support or skilled services ► Alive to home with support or skilled services ► Alive to an inpatient rehabilitation facility ► Alive to chronic care facility such as a nursing home
Reoperation	Return to operating room within index hospitalisation
Non-fatal cardiac arrest	Any successful resuscitation from ventricular fibrillation, sustained ventricular tachycardia, asystole or pulseless electrical activity
Clinician diagnosis of myocardial infarction	Diagnosis of postoperative myocardial infarction based on assessment of responsible clinicians
Myocardial infarction	Diagnosed by an independent Outcome Adjudication Committee using the Fourth Universal Definition of myocardial infarction[55]
Acute myocardial injury	Postoperative troponin concentration that (1) exceeds the 99th percentile upper reference limit for the assay, (2) exceeds the preoperative troponin concentration and (3) is characterised by a rise and/or fall of troponin concentration values[55]
Acute heart failure	Presence of clinical (elevated jugular venous pressure, respiratory rales, crepitations or presence of S3) and radiological (vascular redistribution or interstitial pulmonary oedema or frank pulmonary oedema) findings consistent with heart failure[53]
New clinically important atrial fibrillation	New atrial fibrillation that results in angina, heart failure, symptomatic hypotension, or requires treatment with a rate-controlling drug, antiarrhythmic drug or cardioversion[53]
Acute stroke	Any new focal neurological deficit, suspected to be of vascular origin, with signs/symptoms lasting ≥24 hours[53]
Transient ischaemic attack	Any transient focal neurological deficit that lasted less than 24 hours and is thought to be vascular in origin[53]
Clinician diagnosis of delirium	Diagnosis of postoperative delirium based on assessment of clinicians at hospital where index surgery was performed
New dialysis requirement	New requirement for dialysis during index hospitalisation
Postoperative respiratory failure[56]	The need for tracheal reintubation and mechanical ventilation after extubation (within 30 days after surgery) or need for mechanical ventilation for >24 hours after surgery
Postoperative pneumonia (CDC definition)[56 57]	Two or more serial chest radiographs with one or more of the following (one radiograph is sufficient for patients with no underlying pulmonary or cardiac disease): (1) new or progressive and persistent infiltrates, (2) consolidation and (3) cavitation AND one or more of the following: (1) fever (>38°C) with no other cause, (2) leucopenia (white cell count $<4\times10^9$/L) or leucocytosis (white cell count $>12\times10^9$/L) and (3) altered mental status in adults >70 years with no other cause AND two or more of the following: (1) new onset of purulent sputum or change in character of sputum, increased respiratory secretions or increased suctioning requirements; (2) new onset or worsening cough, dyspnoea, tachypnoea, rales or bronchial breath sounds and (3) worsening gas exchange (hypoxaemia, increased oxygen requirement, increased ventilator demand)
Postoperative acute respiratory distress syndrome (Berlin Criteria)[56 58]	Occurs within 1 week of a known clinical insult or new or worsening respiratory symptoms AND chest imaging shows bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules AND respiratory failure is not fully explained by cardiac failure or fluid overload AND oxygenation requirements ranging from: ► Mild disease with PaO_2:FiO_2 between 200 and 300 mm Hg with PEEP or CPAP ≥5 cm H_2O ► Moderate disease defined by PaO_2:FiO_2 between 100 and 200 mm Hg with PEEP ≥5 cm H_2O ► Severe disease defined by PaO_2:FiO_2 less than 100 mm Hg with PEEP ≥5 cm H_2O
Postoperative pulmonary complication[56]	Defined by the presence of one or more of the following: (1) atelectasis on CT or chest radiograph, (2) pneumonia, (2) acute respiratory distress syndrome and (3) pulmonary aspiration (clear clinical history and radiological evidence) If present, severity should be further classified as: ► None: planned use of supplemental oxygen or mechanical respiratory support only as part of routine care ► Mild: therapeutic supplemental oxygen <0.6 FiO_2 ► Moderate: therapeutic supplemental oxygen ≥0.6 FiO_2, requirement for high-flow nasal oxygen or both ► Severe: unplanned non-invasive mechanical ventilation, CPAP or mechanical ventilation with tracheal intubation
Sepsis	Presence of infection and systemic inflammatory response, which is defined by two or more of the following: core temperature >38°C or <36°C, heart rate >90 beats/min, respiratory rate >20 breaths/min, white cell count $>12\times10^9$/L or white cell count $<4\times10^9$/L
Superficial surgical site infection (CDC definition)[59 60]	Infection within 30 days after the principal operative procedure that involves only skin or subcutaneous tissue of the incision AND one or more of the following is present: (1) purulent drainage from the superficial incision, (2) organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision and (3) superficial incision is deliberately opened by the surgeon AND one or more of the following is present: (1) pain or tenderness, (2) localised swelling, (3) redness and (4) heat.
Deep surgical site infection (CDC definition)[59 60]	Infection within 30 days after the principal operative procedure that involves deep soft tissues AND one or more of the following is present: ► Purulent drainage from the deep incision but not from the organ/space component of the surgical site ► A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localised pain or tenderness, unless the site is culture negative ► An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathological or radiological examination ► Diagnosis of a deep incision surgical site infection by a surgeon or attending physician

Continued

Table 2 Continued

Event	Definition
Organ/space surgical site infection	Infection within 30 days after the principal operative procedure that involves any of the anatomy, other than the incision, which was opened or manipulated during the operation, AND one or more of the following is present: ► Purulent drainage from a drain that is placed through a stab wound into the organ/space ► Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space ► An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation or by histopathological or radiological examination ► Diagnosis of an organ/space surgical site infection by a surgeon or attending physician
Wound disruption	Spontaneous reopening of a surgically closed wound that occurs within 30 days after the principal operative procedure AND one of the following criteria below is present: ► Abdominal site: loss of the integrity of fascial closure (or whatever other closure was performed instead) ► Other surgical sites: total breakdown of the surgical closure compromising the integrity of the procedure
Deep venous thrombosis (DVT)[53]	Any of the following during index hospitalisation: (1) persistent intraluminal filling defect on contrast venography, (2) one or more non-compressible venous segment on B-mode compression ultrasonography and (3) clearly defined intraluminal filling defect on contrast-enhanced CT
Pulmonary embolism[53]	Any of the following during index hospitalisation: ► High probability ventilation/perfusion lung scan ► Intraluminal filling defect of segmental or larger artery on a helical CT scan ► Intraluminal filling defect on pulmonary angiography ► A positive diagnostic test for DVT (eg, positive compression ultrasound) PLUS one of the following: – Low or intermediate probability ventilation/perfusion lung scan – Non-diagnostic (subsegmental defects or technically inadequate study) helical CT scan
Reoperation for bleeding	Surgical intervention (including endovascular procedures) after the index surgical procedure to treat bleeding
Life-threatening bleeding[61]	Classified as (1) bleeding event that was fatal, and event that led to significant hypotension that required inotrope or vasopressor therapy, emergent (within 24 hours) reoperation (other than superficial vascular repair), or intracranial haemorrhage.
Major bleeding[61]	Bleeding event that was not specified under life-threatening bleeding and resulted in any of the following: ► Haemoglobin ≤70 g/L and ≥2 units of red blood cells transfused ► Haemoglobin drop of ≥50 g/L and ≥2 units of red blood cells transfused ► ≥4 units of red blood cells transfused within a 24-hour period ► Any one of the following interventions (ie, embolisation, superficial vascular repair, nasal packing) ► Retroperitoneal, intraspinal or intraocular bleeding

CDC, Centers for Disease Control and Prevention; CPAP, continuous positive airway pressure; CT, computed tomography ; FiO_2, fractional inspired oxygen; PaO_2, arterial oxygen tension (or pressure); PEEP, positive end-expiratory pressure.

9 and 12 months after surgery, research personnel ascertain vital status, administer survey instruments, assess level-of-care needs and identify new health-related events that might impact on disability (table 3).

Surveys administered during follow-up (figure 1) include the WHODAS, SF-12, PHQ-9, PROMIS Pain Intensity Form 1a, PROMIS Pain Interference Short Form 6a and Decision Regret Scale.[39] At the 3-month follow-up assessment, participants also report their freedom from disability relative to their preoperative status on a 15-point global rating scale scored from −7 (a great deal worse) to +7 (a great deal better).[40]

Outcome measures

The primary outcome is the composite of significant new disability or death at 6 months following the index surgery. Significant new disability is defined as a WHODAS score of 12 or greater (≥25%),[10 25] which exceeds the preoperative score by a difference of 2.4 points or greater (absolute increase ≥5%).[26] The primary outcome is assessed at the 6-month follow-up because self-reported functional status should return to baseline in most patients by this point,[12] and the 6-month window preserves a reasonable temporal link between the immediate impact of surgery and patients' subsequent functional status. Death is included as a component of the composite outcome because it is patient-relevant, precludes individuals from otherwise experiencing disability and is arguably the most severe form of disability. Secondary outcomes are (1) significant new disability or death at 1 year after surgery, (2) increased care needs or death at 6 months after surgery and (3) increased care needs or death at 1 year after surgery. Increased care needs are defined as the new need for support or skilled services at home or new need for living in a care facility (eg, nursing home), when compared with the preoperative status.[14]

Statistical analysis

Initially, WHODAS scores (mean, median, SD, IQR), level-of-care needs (proportion) and deaths (proportion) will be characterised at all assessments points. The proportions, along with 95% CIs of participants experiencing the primary and secondary outcomes will be calculated. Standardised differences and bivariate tests (t-test, χ^2 test, Mann-Whitney U test, Fisher's exact test) will then be used to compare the characteristics (ie, preoperative, surgical, in-hospital, postdischarge) of strata defined by the presence or absence of the primary and secondary outcomes.

Multivariable logistic regression models will be used to separately estimate the adjusted association of preoperative characteristics and surgery type with the primary and secondary outcomes. Predictor terms in the models are age, sex, surgery type, comorbidities (coronary artery disease, heart failure, cerebrovascular disease, atrial fibrillation, obstructive pulmonary disease, diabetes,

Table 3 Clinical events ascertained following hospital discharge

Event	Definition
Use of a gait or mobility aid	Use of a device to improve walking pattern, balance or safety while mobilising independently. These devices include canes (walking sticks), crutches or walkers.
Hospital admission	If present, date of admission is documented.
Repeat surgery	If present, date of surgery is documented, as well as whether the surgery is related to the original index surgery.
New diagnosis of cancer (excluding non-melanoma skin cancers)	New diagnosis of cancer (ie, no prior history of this cancer).
Diagnosis of recurrent cancer (excluding non-melanoma skin cancers)	Diagnosis of recurrent cancer (ie, recurrence of a previous cancer for which the patient received curative treatment).
Chemotherapy	If present, start date of treatment is documented.
Radiation therapy	If present, start date of treatment is documented.
Myocardial infarction	Diagnosed by an independent Outcome Adjudication Committee that using the Fourth Universal Definition of myocardial infarction.[55]
Heart failure	Presence of clinical (elevated jugular venous pressure, respiratory rales, crepitations or presence of third heart sound) and radiological (vascular redistribution or interstitial pulmonary oedema or frank pulmonary oedema) findings consistent with heart failure.[53]
Acute stroke	Any new focal neurological deficit, suspected to be of vascular origin, with signs/symptoms lasting ≥24 hours.[53]
Amputation	Amputation procedure after the initial surgery.
New requirement for dialysis	Use of haemodialysis or peritoneal dialysis apparatus.
Days alive at home at 30 days after surgery	Days alive at home at 30 days after surgery is defined as the number of days in the 30 days after surgery where the patient is alive and at home (not in acute care hospital, inpatient rehabilitation facility or chronic care facility). If an individual dies within the 30 days after surgery, the days alive at home value is zero.[62 63]
Falls within the preceding 3 months (assessed at 3, 6, 9 and 12 months after surgery)	An unexpected event in which the participants come to rest on the ground, floor or lower level within the preceding 3 months.[54] Further classified as: 1. None 2. One fall 3. Two or more falls.

liver disease, arthritis, peripheral artery disease, cancer), smoking status and falls history. Restricted cubic splines will be used to assess whether continuous variables conform to model assumptions.[41] All variables will be entered into the models simultaneously. Multicollinearity will be assessed using the variance inflation factor, discrimination will be measured using the c-index and calibration will be assessed by observed versus predicted plots. Model validation will be performed using bootstrap resampling.[41] In supplementary analyses, the models will be separately re-estimated after replacing comorbidities and falls history as predictor variables with frailty status. Frailty is defined by CFS score of 4 or more.[42]

We will use joint modelling to examine repeated WHODAS scores over the postoperative assessments at 1, 3, 6, 9 and 12 months after surgery, while accounting for non-random participant attrition related to deaths during the same follow-up period.[43] Model covariates will include preoperative WHODAS score, age, sex, surgery type, comorbidities (coronary artery disease, heart failure, cerebrovascular disease, atrial fibrillation, obstructive pulmonary disease, diabetes, liver disease, arthritis, peripheral artery disease, cancer), smoking status and falls history. In a supplementary analysis, the joint models will be re-estimated after replacing comorbidities and falls history as predictor variables with frailty status. In sensitivity analyses, we will instead use linear mixed models to examine repeated postoperative WHODAS scores after either excluding any postoperative deaths or assigning a WHODAS score of 48 (100%) to any individual who is deceased at a follow-up assessment.[42]

To supplement findings from the joint models, we will estimate group-based trajectory models to identify potential subgroups of patients with similar patterns of postoperative recovery.[44] Longitudinal latent class mixture models will be used to identify distinct subgroups with similar trajectories in WHODAS scores, while accounting for non-random participant attrition related to postoperative deaths.[45] Posterior probabilities will be used to assign subjects to the appropriate grouping. We will characterise these subgroups with respect to their preoperative, surgical and immediate postoperative (eg, complications) features. In sensitivity analyses, we will re-estimate the group-based trajectory models after either excluding any postoperative deaths or assigning a WHODAS score of 48 (100%) to any individual who is deceased at a follow-up assessment.[42]

Sample size calculation

The sample size is based on robust estimation of a multivariable logistic regression model predicting the primary outcome (significant new disability or death at 6 months after surgery). Based on extrapolation from prior work,[46 47] we estimate an event rate of 13%–18% for the primary outcome. We initially used Monte Carlo simulation (10 000 replications) to estimate the sample size needed to detect clinically relevant effect sizes (ie, adjusted ORs) in a multivariable logistic regression model.[48] We estimated that 1900 participants are needed to detect an adjusted OR of 1.5 for a binary predictor variable in a model with 20 parameters, based on underlying assumptions of an outcome event rate of 13%, power exceeding 80% and two-sided alpha of 0.05. To account for a 5% drop-out rate, the total target sample size for recruitment was increased to 2000. Recent research on sample sizes to develop robust prediction models,[49] which was published after initiation of the FIT After Surgery study, suggests that this sample size estimate is likely conservative. Based on the same assumption of an outcome event rate of 13%, these newer methods indicate that 1846 participants are required to estimate a robust model that has up to 30 parameters, and conservatively explains 25% of outcome variance.[49]

Study management and funding

The Applied Health Research Centre at St. Michael's Hospital—Unity Health Toronto (Toronto, Ontario, Canada) is responsible for the overall coordination of the FIT After Surgery study. Participating study investigators and their respective roles are listed in the online supplemental appendix. All study data were collected and managed using web-based Research Electronic Data Capture (REDCap) tools hosted at Unity Health Toronto.[50 51] The FIT After Surgery study is funded by peer-reviewed grants from the Canadian Institutes of Health Research and the Physicians Services Incorporated (PSI) Foundation.

Study status

Participant recruitment into the FIT After Surgery study began in December 2019. All participant recruitment was placed on hold in March 2020 because of the COVID-19 pandemic and its impact on clinical research activities. Recruitment was gradually restarted in October 2020, with completion of 1-year follow-up anticipated in 2023. The study involves 16 centres across six Canadian provinces: British Columbia, Alberta, Manitoba, Ontario, Quebec and Nova Scotia.

Substudies

We have developed a formal process for members of the FIT After Surgery study investigator team to propose, design and lead secondary analyses and substudies in this large multicentre cohort of older adults having major elective non-cardiac surgery. Several studies have already been prespecified, including a nested cohort study to evaluate the association of self-reported disability with preoperative and postoperative measurements from wearable activity monitors, a nested cohort study to evaluate the association of caregiver burden with postoperative recovery in older adults with frailty, and a secondary analysis of the main FIT After Surgery study dataset to develop a clinical prediction tool for new significant postoperative disability.

Patient and public involvement

A representative of the Canadian Association of Retired Persons, which is a public advocacy organisation representing older Canadian adults, was involved in reviewing the study objectives and rationale, providing feedback on the study design and joining as a coapplicant in grant funding applications. Two older adults with lived experience of having surgery provided feedback on study materials, recruitment strategies and proposed study questionnaires. At the conclusion of the study, we plan to meet with older adults and representatives of related advocacy organisations to help better interpret the study results and finalise a knowledge translation strategy.

ETHICS AND DISSEMINATION

The FIT After Surgery study has been approved by the following research ethics boards: Unity Health Toronto Research Ethics Board, Providence Health Care Research Ethics Board, Nova Scotia Health Authority Research Ethics Board, University of Calgary Conjoint Health Research Ethics Board, University of Alberta Research Ethics Office and University of Manitoba Biomedical Research Ethics Board. Through Clinical Trials Ontario, the Unity Health Toronto Research Ethics Board is responsible for ethics approval at all study sites in Ontario, Canada. All participants provide informed consent at the time of recruitment to the study. The study poses minimal additional risk to study participants. A possible safety issue is a concerning response in the PHQ-9 questionnaire (possible risk of significant depression or suicidal ideation), the AD8 interview (possible risk of significant cognitive decline) or the CAGE questionnaire (significant risk of alcohol use disorder). If a participant reports any such concerning response, research personnel at the study site inform the participant's primary care provider or surgeon to facilitate appropriate follow-up as part of standard clinical care.

The results of the FIT After Surgery study will be published in peer-reviewed journals and presented at both national and international conferences. Publication of the primary results is anticipated to occur in 2024. We plan for end-of-grant knowledge translation that involves identifying key messages from the study for our target audiences; seeking out interested, influential and credible individuals or organisations to act as sources of the messages; and using a knowledge translation strategy

based on best evidence.[52] At the conclusion of the study, we plan to meet with key stakeholders (older adults, clinicians, researchers, health policy makers) to help better interpret the study results and finalise a knowledge translation strategy. We have already liaised with stakeholders representing researchers and clinicians (Canadian Frailty Network), older adults (Canadian Association of Retired Persons) and policy makers (Ontario Health, Cancer Care Ontario), and our study team includes members who represent several of these stakeholder organisations.

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Contributors DNW, SMHA, KSL, MTEP, GL, CDM, ACW and DIM contributed to the conception and design of the study. DNW, KSL, TRC, JFD, SE, EH, JMvV and DIM contributed to the acquisition of study data. DNW, SMHA, KSL, MTEP, TRC, JFD, SE, EH, GL, CDM, JMvV, ACW and DIM contributed to the analysis and interpretation of the study data. DNW wrote the first draft of the manuscript. DNW, SMHA, KSL, MTEP, TRC, JFD, SE, EH, GL, CDM, JMvV, AW and DIM revised the manuscript critically for important intellectual content. DNW, SMHA, KSL, MTEP, TRC, JFD, SE, EH, GL, CDM, JMvV, AW and DIM have read and approved the final version of the manuscript to be published.

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Competing interests DNW is a member of the Scientific Advisory Board for Surgical Safety Technologies and has received honoraria from Edwards Lifesciences within the last 5 years. KSL is Co-Principal Investigator of an observational study on medical cannabis funded by Shoppers Drug Mart. DM has received advisory board honoraria and/or consulting fees from Amgen, AstraZeneca, BioAge, Boehringer Ingelheim and PhaseBio, and honoraria for Data Safety and Monitoring Board membership from Beth Israel Deaconess Medical Center, Cerus and Takeda, all outside the submitted work.

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

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the following research ethics boards: Unity Health Toronto Research Ethics Board, Providence Health Care Research Ethics Board, Nova Scotia Health Authority Research Ethics Board, University of Calgary Conjoint Health Research Ethics Board, University of Alberta Research Ethics Office and University of Manitoba Biomedical Research Ethics Board. The central coordinating site ethics board is the Unity Health Toronto Research Ethics Board (CTO Project ID 1654). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study. Not applicable.

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