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PREPARE trial: a protocol for a multicentre randomised trial of frailty-focused preoperative exercise to decrease postoperative complication rates and disability scores

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ABSTRACT

Introduction Frailty is a strong predictor of adverse postoperative outcomes. Prehabilitation may improve outcomes after surgery for older people with frailty by addressing physical and physiologic deficits. The objective of this trial is to evaluate the efficacy of home-based multimodal prehabilitation in decreasing patient-reported disability and postoperative complications in older people with frailty having major surgery.

Methods and analysis We will conduct a multicentre, randomised controlled trial of home-based prehabilitation versus standard care among consenting patients >60 years with frailty (Clinical Frailty Scale≥4) having elective inpatient major non-cardiac, non-neurologic or non-orthopaedic surgery. Patients will be partially blinded; clinicians and outcome assessors will be fully blinded. The intervention consists of ≥3 weeks of prehabilitation (exercise (strength, aerobic and stretching) and nutrition (advice and protein supplementation)). The study has two primary outcomes: in-hospital complications and patient-reported disability 30 days after surgery. Secondary outcomes include survival, lower limb function, quality of life and resource utilisation. A sample size of 750 participants (375 per arm) provides >90% power to detect a minimally important absolute difference of 8 on the 100-point patient-reported disability scale and a 25% relative risk reduction in complications, using a two-sided alpha value of 0.025 to account for the two primary outcomes. Analyses will follow intention to treat principles for all randomised participants. All participants will be followed to either death or up to 1 year.

Ethics and dissemination Ethical approval has been granted by Clinical Trials Ontario (Project ID: 1785) and our ethics review board (Protocol Approval #20190409-01T). Results will be disseminated through presentation at scientific conferences, through peer-reviewed publication, stakeholder organisations and engagement of social and traditional media.

Trial registration number NCT04221295.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Adequately powered and blinded for patient-centred outcomes.
⇒ Enhanced prehabilitation intervention with efficacy in single-centre trials
⇒ Multicentre trial will enhance generalisability.
⇒ Complex intervention, possible risk of intervention contamination.

INTRODUCTION

Rates of major surgery are growing most rapidly in older people.[1] Frailty, a multidimensional state that develops due to age-related and disease-related deficits that accumulate across the lifespan is present in 30%–40% of older surgical patients.[2–5] When present before surgery, frailty is associated with a more than twofold increase in rates of new patient-reported disability, major complications, readmission, non-home discharge and death.[6–11] One in five older people with preoperative frailty develop a new patient-reported postoperative disability.[2] Approximately 50% experience a complication,[12] which mediates the majority of the frailty-mortality association.[13] Accordingly, experts and guidelines suggest that optimising physical and physiological status before surgery could reduce adverse postoperative outcomes for older people with frailty.[14–16]

Prehabilitation involves actively preparing patients for surgery through exercise, nutritional support, psychocognitive intervention or a combination of these modalities.[17] A recent umbrella review identified that consistent, low to very low certainty, evidence supports a beneficial effect of prehabilitation on complication rates, non-home discharge, length of stay and functional recovery.[17] However, clearly lacking from the prehabilitation evidence base are multicentre randomised trials. This knowledge gap is

particularly pertinent to people with frailty, as few trials have specifically enrolled patients with frailty.[18 19] While prehabilitation could be an optimal approach to enhance the decreased reserves inherent in living with frailty, efficacy in improving functional outcomes and complication rates has only been demonstrated among individuals adequately adherent to their prescribed intervention.[20–22]

To address the high-priority knowledge gaps specific to prehabilitation of older surgical patients with frailty, a multicentre randomised trial of a prehabilitation intervention that optimises adherence, addresses physical and nutritional deficits, and meets the needs of vulnerable older people with frailty is required. Therefore, we will conduct the PReoperative Exercise to decrease PostoperAtive complication Rates and disability scorEs (PREPARE) Trial. This multicentre randomised trial of a home-based multimodal prehabilitation programme, compared with standard care, will test the hypothesis that multimodal prehabilitation decreases postoperative complications and reduces patient-reported disability (primary outcomes), while improving secondary outcomes (lower limb function, frailty, resource use, quality of life, survival).

METHODS AND ANALYSIS

Study design and setting

We will conduct a clinician and assessor-blinded, partially patient-blinded, individual patient parallel-arm randomised controlled trial of home-based multimodal prehabilitation compared with standard perioperative care in older adults living with frailty undergoing elective, inpatient major non-cardiac, non-neurologic, non-orthopaedic elective surgery at 10 or more Canadian community and academic hospitals. The Ottawa Hospital will serve as the coordinating centre. This protocol is reported in keeping with the Standard Protocol Items: Recommendations for Intervention Trials guidelines.[23] Research Ethics Board (REB) approval has been granted from Clinical Trials Ontario (CTO, Project ID: 1785), The Ottawa Health Sciences Network-REB (Protocol #20190409-01T) and will be granted from all participating centres prior to the commencement of recruitment. Eligibility criteria are outline in box 1.

Patient and public involvement

Our trial was developed to be aligned with patient-centred and community-centred priorities for research, and uses an integrated knowledge translation approach where we partnered with patients and knowledge users from conception of our protocol.[24] James Lind Alliance priority setting partnerships[25–27] further informed our protocol through defined priority areas for perioperative research, including: (1) improving the care of older people having surgery; (2) the role of exercise in improving surgical outcomes; (3) the role of exercise in managing frailty and (4) improving home based care for older people with frailty.[25 27 28] Patient partners have been engaged in all stages of the protocol development and study oversight. Patient experience with the intervention will be measured quantitatively and qualitatively. Study results will be disseminated to participants through traditional and social media, as well as using newsletters.

Box 1 Inclusion and exclusion criteria for the PReoperative Exercise to decrease PostoperAtive complication Rates and disability scorEs trial

Inclusion criteria
- ⇒ Age ≥60 years.
- ⇒ Elective inpatient surgery.
- ⇒ Expected surgery date between 3 and 12 weeks from enrolment.
- ⇒ Clinical Frailty Scale (CFS) score of ≥4/9*.

*The CFS is a 9-point global frailty scale based on clinical evaluation and judgement of an individual's mobility, energy, physical activity and function.[3]

Exclusion criteria
- ⇒ Inability to speak English or French.
- ⇒ Comorbidity preventing assessment or understanding of questionnaires.
- ⇒ Unable to be contacted by telephone.
- ⇒ Unwilling to participate in exercise programme.
- ⇒ Cardiac, neurological or orthopaedic procedure.
- ⇒ Palliative surgery (ie, without curative intent).
- ⇒ Any of the following cardiovascular conditions:
  - ⇒ Severe valvular heart disease that limits a patient's ability to ambulate on level ground, or is associated with syncope or dyspnoea.
  - ⇒ Severe cardiac dysrhythmias that limits a patient's ability to ambulate on level ground, or is associated with syncope or dyspnoea.
  - ⇒ Recent myocardial infarction (within the 6 weeks prior to enrolment, based on the Heart & Stroke Foundation's HeartWalk Programme).

Items from the WHO Trial Registration Data Set are reported in table 1.

Intervention

Our intervention is a structured, home-based, multimodal prehabilitation programme that has been enhanced using integrated knowledge translation methods since successful implementation in our pilot trial.[20 21] The protocol was developed with kinesiologists, exercise scientists and dieticians: (1) was informed by a protocol with efficacy in improving function for surgical patients without frailty,[29–31] (2) tailors movements to the needs and safety of people with frailty, (3) integrates feedback from pilot trial participants obtained through structured qualitative and quantitative assessment,[20] (4) provides nutritional prehabilitation informed by malnutrition risk and (5) integrates evidence-based and theory informed strategies to enhance adherence.[32–34] Our data demonstrate that the intervention can be feasibly implemented; 95% of older people with frailty who are randomised to exercise participate in the programme. Among enrolled patients, 87% report that it is easy to follow, enjoyable, well suited to their needs and that lack of experience with exercise was not a barrier to participation.[35]

Table 1 All items from the WHO trial registration data set

Data category	Information
Primary registry and trial identifying no	ClinicalTrials.gov NCT04221295
Date of registration in primary registry	9 January 2020
Secondary identifying numbers	Not applicable
Source(s) of monetary or material support	The Canadian Institutes of Health Research The Ottawa Hospital Academic Medical Organization
Primary sponsor	The Ottawa Hospital Research Institute
Secondary sponsor	Investigator-led, Dr. Daniel McIsaac
Contact for public queries	DM, dmcisaac@toh.ca
Contact for scientific queries	DM, dmcisaac@toh.ca
Public title	The PREPARE Trial: Exercise Before Surgery to Improve Recovery in Older People With Frailty
Scientific title	The PREPARE Trial: a protocol for a parallel arm multicentre randomised trial of frailty-focused PREPARE
Countries of recruitment	Canada
Health condition(s) or problem(s) studied	Frailty, major surgery
Intervention(s)	Tri-modal prehabilitation
Key inclusion and exclusion criteria	Ages eligible for study: ≥60 years Sexes eligible for study: both Accepts health volunteers: no
	Inclusion criteria: adult patient (≥60 years), inpatient, major elective surgery date between 3 and 12 weeks from enrolment, Clinical Frailty Score (≥4/9)
	Exclusion criteria: unable to communicate in written or oral form in official languages serviced by The Ottawa Hospital (English or French), unreachable by telephone, major cardiac risk factors, cardiac, neurological or orthopaedic procedures, scheduled to undergo surgery in fewer than 3 weeks from randomisation
Study type	Interventional
	Allocation: randomised intervention model. Parallel assignment masking: double blind (investigator and outcome assessors)
	Primary purpose: prevention
Date of first enrolment	2 March 2020
Target sample size	750
Recruitment status	Recruiting
Primary outcome(s)	In-hospital complications, patient-reported disability
Key secondary outcomes	Function, patient-reported health related quality of life, participant feedback, all-cause mortality

PREPARE, PReoperative Exercise to decrease PostoperAtive complication Rates and disability scorEs.

The exercise component will be prescribed as 1 hour sessions, performed a minimum of three times per week for 3 weeks, consisting of: (1) strength training; (2) aerobic exercise and (3) flexibility. Participants will be provided with an exercise programme booklet, a calendar for tracking exercise, three instructional videos (strength, seated cardio, standing cardio), a pedometer and graded elastic resistance bands. After enrolment and allocation, intervention participants will receive a telephone-assisted education session on the exercise programme. Participants will be further supported by our experienced central team using weekly phone calls to monitor safety, encourage adherence and provide advice on exercise progression.

Strength training will consist of 1 set of 10 repetitions of each exercise: push-ups (modified to the individual's level of function as wall push-ups or knee push-ups), seated row, chest fly, deltoid lift, biceps curls, triceps extensions, quadricep exercises, hamstring curls, standing calf raises, modified chair-seated abdominal crunches. The participants will be provided with an elastic resistance band to complete these exercises at home. For aerobic activity, participants will be asked to walk at moderate intensity, or engage in a personalised moderate intensity aerobic activity (eg, swimming, cycling) for 20 min sessions. After the first week, the individual's average daily step count (or distance cycled or swam) is used to recommend a 10% increase in daily step count (or distance) each week. People with frailty typically have low baseline step counts,[36] and a 10% increase per week is considered to be a safe, meaningful and achievable method to personalise activity goals.[37] Lastly, the flexibility component consists

of 6 stretches each to be held for 20 s, done for 2 repetitions. The stretches target the chest, arms, legs and trunk.

Participants will be screened for risk of malnutrition using the Canadian Nutrition Screening Tool (CNST), a simple and reliable nutrition screening tool that addresses involuntary weight loss and reduced food intake.[38] Participants will receive a pamphlet for nutritional advice and coupons for protein supplements (we have no commercial or research involvement or relationships with any supplement manufacturer). The trained central team will provide participants with structured nutrition advice regarding energy and protein requirements based on their participation in the intervention and their specific responses to the CNST. Theory-driven behaviour modification techniques will be applied including providing education about nutrition, goal-setting conversations and structured responses to commonly encountered barriers to adequate dietary intake in older adults to promote adequate protein intake and support nutritional status.[39] Nutrition will be monitored and supported during weekly adherence calls by the central team and supervised by a registered dietician (CG).

Control condition

To support blinding of control participants, they will receive age-standardised recommendations for activity and healthy eating. Unlike the intervention group, no active support, logs or regular contact will be available for control participants. Specific recommendations will be communicated through provision of paper copies of the WHO Recommendations for Physical Activity for People>65 Years pamphlet and A Guide to Healthy Eating for Older Adults.[40]

Preoperative, in-hospital and postoperative care

All other aspects of perioperative management will be at the discretion of treating clinicians. There will be no standardisation of intraoperative anaesthesia or surgical care, and participation in perioperative care processes, such as enhanced recovery after surgery programmes, will be dictated by local practice.

Outcomes

This trial has two primary outcomes, which were identified based on (1) prospective prioritisation surveys of older surgical patients[2 41]; (2) systematic reviews of existing efficacy data[42–45] and (3) engagement with our patient partners and knowledge users. Through this process, we identified reduction in postoperative patient-reported disability scores and avoidance of in-hospital postoperative complications as important and mechanistically relevant outcomes. An effect of the intervention on at least one of the two primary outcomes would be indicative of benefit.

To measure patient-reported disability 30 days after surgery, we will use the WHO Disability Assessment Schedule 2.0 (WHODAS). The WHODAS is a patient-reported disability scale that assesses limitations in six major life domains (ie, cognition, mobility, self-care, social interaction, life activities, participation in society),[46 47] has been validated in surgical patients[48] (and other conditions,[49–54] and was identified by older surgical patients as a high-priority outcome.[41 55] Each questionnaire item is scored on a Likert scale ranging from 0 to 4. The sum of the responses provides the WHODAS Disability Score (range: 0–48), which is then expressed as a percentage of the maximum possible score (ie, range 0%–100%). People who die prior to follow up will be scored as completely disabled. Based on normative data, an absolute mean difference of 8% for WHODAS scores is meaningful,[39] whereas subsequent data in surgical patients suggests a minimally important absolute difference of 5%.[56]

In-hospital postoperative complications will be identified using the Postoperative Morbidity Survey (POMS), a prospectively administered instrument designed to identify significant in-hospital complications in key organ systems,[57 58] previously used in many prospective studies.[20 59–68] The instrument will be administered on postoperative days 3, 5 and discharge, and any patient experiencing a complication at any assessment point, or who dies in hospital, will be categorised as having experienced a complication for this primary outcome. The POMS contains 18 items addressing nine domains (ie, pulmonary, infectious, renal, gastrointestinal, cardiovascular, neurological, haematological, wound and pain), however, based on current data and understanding of prehabilitation's mechanism,[17] the pain domain will not be included in the primary outcome definition, as previously described.[21] In validation studies, the POMS has high inter-rater agreement (kappa=0.94–1.0), acceptability, and demonstrated construct validity.[57] At each assessment, the severity of incident complications will be graded using the updated Clavien-Dindo Classification.[69] The study flow and timeline of outcome assessments are shown in figure 1.

Secondary outcomes will reflect five specific domains: (1) function total postoperative pedometer-counted steps[70–72] in the 30 days after surgery, the 5 Times Sit to Stand (5TSTS)[73] and the Katz Index measure of activities of daily living (both at hospital discharge)[74]; (2) health-related quality of life (HRQol; EQ-5D-5L[75–77]; (3) mortality (deaths and death dates will be identified in-hospital or through telephone follow-up); (4) healthcare utilisation discharge disposition (home, home with support, rehabilitation, long term care, death), 30-day readmissions; linkage to health administrative databases will support long-term follow-up, allowing capture of health system costs,[78] emergency department visits and subsequent long-term care admissions in the year after surgery[79] and (5) patient experience with prehabilitation (Theoretical Domains Framework[80 81] participant survey to identify barriers and facilitators to participation in prehabilitation for intervention group participants).

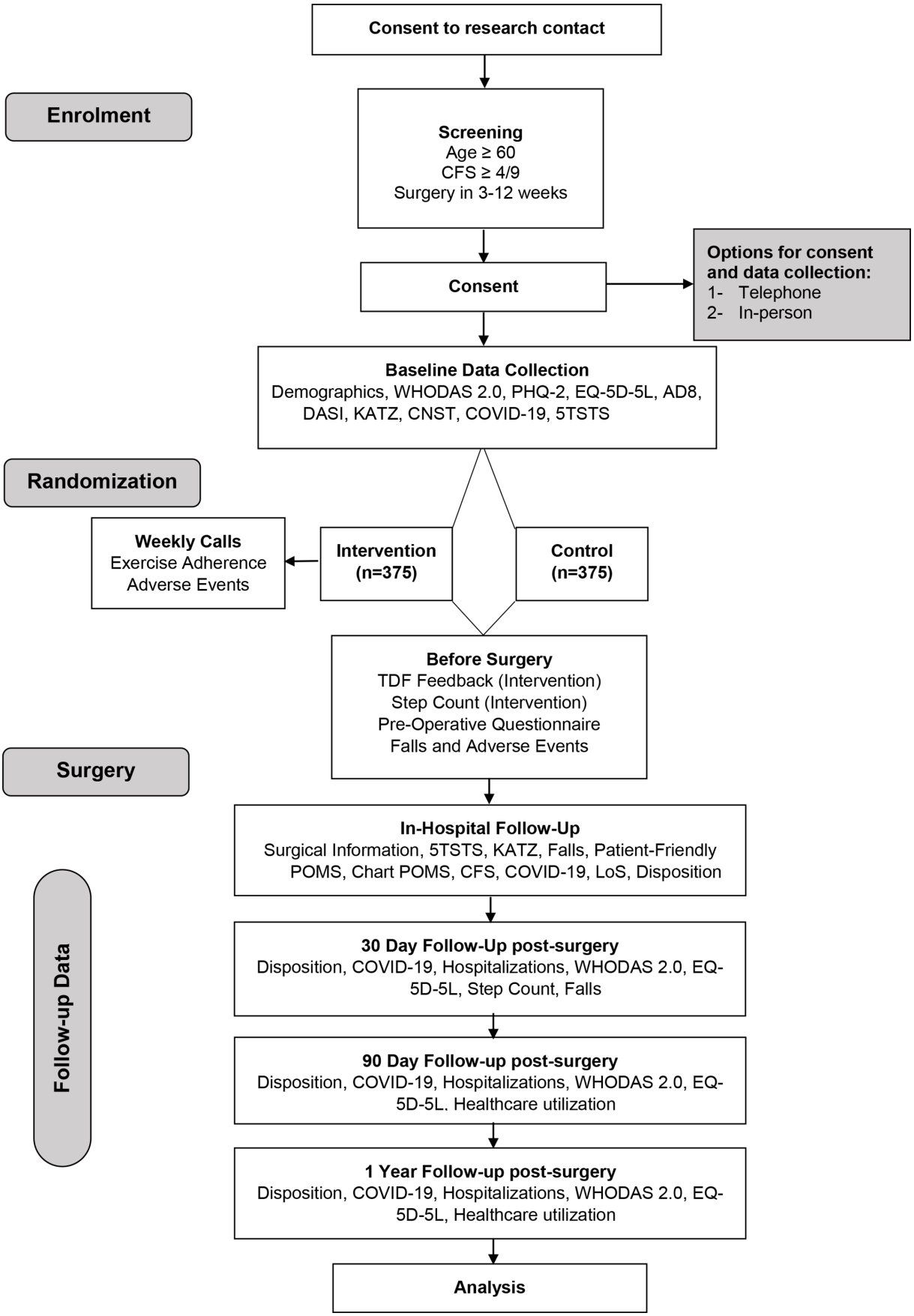

Figure 1 Study flow. CFS, Clinical Frailty Scale; CNST, Canadian Nutrition Screening Tool; DASI, Duke Activity Status Index; eLOS, expected length of stay; PHQ2-Personal Health Questionnaire; POMS, Postoperative Morbidity Survey; 5TSTS, 5 Times Sit to Stand; TDF, Theoretical Domains Framework; WHODAS, WHO Disability Assessment Schedule.

Sample size

Our total sample size of 750 participants (375 per arm) is driven by our binary primary outcome of in-hospital postoperative complications. We have assumed a control arm complication rate of 55% (ie, proportion of patients with at least one complication), which is informed by data from our prospective cohort study[3] and by systematic reviews.[12] In keeping with our intention-to-treat (ITT) analysis, a sample size of 750 participants achieves 90% power to detect our target difference (ie, a relative difference of 25%) using an unpooled Z-test with a two-sided alpha level of 0.025. This calculation accounts for a 10% non-compliance factor largely consisting of randomised participants not having their planned surgery to reflect the real-world clinical scenario.[63] For the continuous coprimary outcome (ie, WHODAS Disability Score at 30 days) this sample size achieves 98% power to detect a minimum clinically important difference of 8 points on a 100-point scale using an analysis of covariance (ANCOVA) at the two-sided alpha level of 0.025. This calculation assumes a common SD of 25, a correlation between baseline and postoperative score of 0.4[3] and accounts for 8% missing data at 30 days and 10% intervention non-compliance. A Bonferroni correction was applied to maintain the overall type I error rate across the two primary outcomes at 5%.

Recruitment

Participants will be recruited either in person from surgical or anaesthesia clinics, or via telephone. Following surgical assessment and confirmation of the decision to operate, patients who consent for research contact, and who meet all inclusion criteria except for frailty score, will be assessed by a trained clinician or clinical assistant using the Clinical Frailty Scale (CFS).[82] Patients who score >4/9 on the CFS will then be offered the opportunity to provide written informed consent or verbal consent, respectively (see online supplemental file 1).

Assignment of the intervention

The random allocation sequence will be computer-generated by an independent biostatistician using permuted blocks of randomly varying lengths, stratified by centre, cancer versus non-cancer surgery, and consent method (in-person vs telephone). Study personnel will access the randomisation sequence via a central secure internet-based application to ensure allocation concealment.

Blinding

Clinicians and outcome assessors will be masked to potential treatment allocation groups. This will partially mask participants as they will be informed that they are being enrolled in a study to evaluate activity interventions before surgery.

Data collection and management

A standardised Electronic Data Capture (EDC) system specifically developed for this study will be used for data collection. Data collection will be completed by research personnel or the site investigator either in-person or over the telephone. Postdischarge data will be collected via telephone by authorised research staff at the central coordinating centre and subsequently entered in the EDC. Appropriate security measures will be taken to authorise study site personnel using unique usernames and passwords prior to entering any data in the EDC. The study data will be housed on a secure in-house server in a privacy legislation compliant manner throughout the duration of the study and up to 10 years after study completion.

Participants will keep a daily log of prehabilitation activities during the exercise prehabilitation phase. When participants cannot be reached by telephone on a given week, participant diaries will be entered into the EDC after receipt by the study team.

We expect rare scenarios where patients are initially scheduled for surgery, but postrandomisation their procedure is either cancelled or substantially delayed. Where patients do not undergo surgery within 12 weeks of enrolment, postenrolment day 84 will be defined as the surgery date to facilitate subsequent outcome collection and to avoid postrandomisation exclusions. In the case of prehabilitation, where the intervention could plausibly impact future need for surgery, postrandomisation exclusions could bias ITT results.[83] To support sensitivity analyses, all study outcomes will also be collected relative to the delayed surgery data should the planned surgery be scheduled at a point after 84 days postenrolment.

Data analysis

Primary analyses will follow ITT principles, defined as the analysis of all randomised participants according to their allocated arm.[83] Descriptive statistics (mean and SD for continuous variables or median and IQR for skewed distributions, and frequency and proportion for categorical variables) will be used to report characteristics of participants in each arm at baseline.

In-hospital complications (coprimary outcome) will be analysed using logistic regression to yield ORs and 97.5% CIs. The analysis will include fixed terms for study arm, stratification factors (centre, cancer surgery, consent method) and prespecified covariates (as adjustment for known prognostic factors can substantially increase power[84–86]: age, sex, surgery type, malnutrition risk and frailty score. A random intercept will account for the centre effect. Absolute risk differences and 97.5% CIs will also be reported.

WHODAS Disability score at 30 days (coprimary outcome) will be analysed using mixed-effects regression with the baseline measure entered as a covariate,[87] together with fixed terms for the stratification factor and the prespecified covariates listed above. A random effect for centre will account for the multicentre trial design. The intervention effect will be expressed as an adjusted mean difference with 97.5% CI. Secondary repeated measures analyses of all disability score measurements (up to 365 days) will use restricted maximum likelihood estimation and model the covariance matrix to account

for correlation in the four repeated measures over time. The model will constrain differences between the arms at baseline[87] by including fixed terms for time and arm by time interaction in addition to the covariates specified above and the random centre effect. The difference between the treatment and control arms at 90 and 365 days will be estimated using adjusted least square mean differences and confidence intervals.

All adjusted secondary analyses will account for the stratification factors and covariates specified in the primary analysis and centre effects. HRQol measures will be analysed as described for disability score. Step counts will be analysed using linear regression. Time to hospital discharge will be analysed using Cox regression with in-hospital mortality as a competing risk. Overall survival will be analysed using Cox regression. Discharge disposition will be analysed using ordinal logistic regression. Health system outcomes (readmissions, emergency department visits and subsequent long-term care admissions) will be analysed using logistic regression. Binary safety outcomes will be analysed as described for complications or exact methods if event numbers are small. Cost analysis will use log-gamma regression.[88] From the perspective of Canada's healthcare system, we will conduct a cost–utility analysis to assess whether exercise prehabilitation offers value for money. Healthcare utilisation and the efficacy of the intervention will be obtained from the trial. We expect attrition to be low; nevertheless, to account for any missing data in our ITT analyses, all eligible patients will be included in all analyses and multiple imputation will be used to maintain power and attenuate biases related to missing data.

Additional analyses will involve a per-protocol analysis (individuals who had their planned surgery and who completed >75% prescribed exercise sessions will be considered the per protocol population). The primary outcomes will be analysed in prespecified subgroups that we postulate may have differing responses to the intervention: sex, age (<75 vs >75,[89] cancer, frailty (4 vs >5). Compliance rates will be compared by sex. These analyses will be conducted by including interaction terms between the subgroup indicator variables and the intervention.

Ethics and dissemination

If the participant is recruited over the telephone, each participant will be read the informed consent form by a trained research assistant in addition to being given the opportunity to read it via email, consider and ask questions about the information in the informed consent form. The trained research assistant must obtain verbal informed consent from the participant before any study procedures occur. At the next available opportunity, the participant will provide their written informed consent. If the participant is recruited in person, each participant will have the opportunity to read the informed consent, consider and ask questions. The trained research assistant must obtain written informed consent or verbal consent from the participant before any study procedures occur. Any modifications to the protocol which may impact on the conduct of the study, potential benefit of the patient or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures or significant administrative aspects will require a formal amendment to the protocol. Such amendments will be reviewed and approved by The Ottawa Health Sciences-Network Research Ethics Board.

Dissemination plans will include local, national and international presentations at scientific conferences, as well as submission to peer-reviewed scientific journals. Press releases will engage lay media, and social media will be further leveraged to disseminate results. Development of brief overviews and visual abstracts will occur and will be shared with study partners, patients and knowledge users.

Confidentiality

Patients' data will be anonymised using a study identification number that will be stored using a protected file separated from the research data. This file will be stored on a secured hospital server where only the researchers in this study will have access to the research data.

Monitoring

An external data and safety monitoring board has been established. All adverse events that occur after enrolment during physical assessments (5TSTS) and during or within 24 hours of participants in the exercise prehabilitation intervention will be documented. Serious adverse events that the principal investigator deems related to the study protocol will be reported to the REB as soon as possible. Local protocols mandate that reporting occur within 7 days if the study-related serious adverse event is unexpected and involves greater risk. Adverse events related to the participants' underlying condition(s) and related treatment will not be collected as part of this study.

The coordinating centre will conduct monitoring sessions to review regulatory and study files, including monitoring of primary outcome data.

DISCUSSION

Older people with frailty are a growing and vulnerable segment of the surgical population and are underrepresented in existing studies.[2 6 7 90 91] Prehabilitation is a high-priority intervention that is particularly relevant to people with frailty given their physical and physiologic vulnerabilities.[4] This multicentre randomised controlled trial will address important knowledge gaps for improving postoperative outcomes for older surgical patients with frailty. This trial will enhance generalisability of findings and will be appropriately powered for important, patient-oriented outcomes including disability and complications.[55 92]

Limitations

There are potential limitations with this trial, many of which we aim to mitigate in our protocol. Adherence to exercise programmes can be low, particularly for older adults with complex health conditions.[93] To improve adherence, our home-based programme has been revised, enhanced and personalised based on feedback from participants in the pilot study. Generalisability will be limited to patients with an expected surgery date at least 3 weeks from the decision to proceed with surgery.

Standardisation of assessments and data collection can be challenging across sites in a multicentre trial. To address this, we have developed training modules to conduct assessments using the CFS[82] to standardise inclusion/exclusion criteria, and a training module to collect primary outcome using the POMS tool. Our coordinating centre will also centralise teaching, coaching, adherence calls and modifications for intervention arm participants. The central team will also handle all follow-up calls and out of hospital data collection.

The current COVID-19 pandemic poses challenges with clinical recruitment and certain trials being put on hold. To address this, our study offers telephone consent as an option. Further, the home-based nature of the intervention is feasible at any time and aligns with the needs and wishes of older people. The consent process will be accounted for in analysis.

There are always risks with participating in exercise programmes, particularly for older adults with frailty. Exercises will be introduced in a graded fashion, and the trained research team will assess for safety events weekly during the intervention phase. There were no reportable serious adverse events in the pilot study.

CONCLUSION

The PREPARE trial will evaluate the efficacy of a pilot-tested, home-based multimodal prehabilitation programme in decreasing patient-reported disability scores and postoperative complications in older people with frailty having major surgery. Recruitment initially commenced in March 2020 but was suspended until November 2020 due to the COVID-19 pandemic. The proposed study will produce generalisable findings directly relevant to the priorities of older adults having surgery.

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Contributors DIM is the principal investigator. DIM was involved in the conception and design of the study and initial draft of the protocol. JN provided her expertise in kinesiology and contributed to the knowledge needed for the prehabilitation program. HM, LL, ML, GB, AH and SG provided their experience in epidemiology, quality improvement, and clinical practice to the study design and procedures, and writing of the protocol. BP provided her knowledge for the care of aging patients and provided insight into the intervention design. AF contributed heavily to the study design and methodology. CSB contributed to the study design and the details of the intervention and control groups. CVW was involved in the study methodology and provided his expertise on data linkage. MT developed the analysis plan. CM provided mentorship oversight and helped draft the protocol. All authors, including the PREPARE Trial Investigators, have critically reviewed and approved the final protocol.

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Competing interests None declared.

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

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