STATISTICAL ANALYSIS PLAN

Description of the Statistical Methods

All data will be analysed used RStudio.

Baseline data:

Descriptive statistics will be presented to summarise the distribution of baseline variables across study groups. Participant characteristics information will include age, time since and age at menopause, cancer characteristics (e.g., cancer stage), chemotherapy regime details, ethnicity, and socioeconomic characteristics (e.g., employment status, and education). All continuous data will be reported as means plus standard deviations, if determined to be normally distributed (assessed via Shapiro-Wilks and visual inspection of Q-Q plots). Otherwise, data will be presented as medians plus interquartile ranges (IQR). All categorical data will be presented as frequencies and percentages.

Intervention feasibility outcome data:

1) Study recruitment rates: the study will be considered feasible if we recruit four patients per month (or 40 patients in 10 months).
2) Study retention rates: The study will be considered feasible if ≥70% (30 patients) of the sample complete post-intervention testing [(N randomised/N completing post-intervention testing) x 100]
3) Adherence to the exercise intervention: The intervention will be considered feasible if participants complete ≥67% (at least 2 out of 3 sessions per week) of the prescribed number of exercises at 12-week follow-up [For each participant: (N prescribed exercise sessions/N exercise sessions attended) x 100%].

Secondary outcome data analysis:

Measures of exercise compliance (Nilsen et al., 2018):

- Patients' adherence to remotely supervised vs. unsupervised exercise sessions (i.e., number of sessions attended or reported).
- Planned dose of exercise training per week vs. patients' completed dose per week.
- Cumulative planned dose vs. patients' cumulative completed dose.

- Relative dose intensity (total “delivered’’ cumulative dose divided by the total planned cumulative dose).
- Loss-to-follow-up.
- Number of patients who permanently discontinued exercise intervention and reason for discontinuation.
- Number of patients who interrupted the exercise intervention (i.e., number of participants who stopped exercising for more than 1 week) and reason for interruption.
- Number of patients missing at least three consecutive sessions.
- Dose modification: number of sessions requiring dose reduction (i.e., target duration not met) during training and the total number of sessions requiring dose modification.
- Exercise intensity modification: number of sessions requiring the intensity of at least one session to be modified because of a pre-exercise screening indication (e.g., fatigue and time constraints).

Exercise safety:

Safety of physical activity will be assessed by recording the number of adverse events occurring during exercise testing, supervised exercise training, and unsupervised exercise training.

Adverse events will be recorded on a standardised data collection form. Study participants will be asked about any identifiable adverse events (e.g., medical events, a fall, severe breathlessness, knee or back pain, new soreness lasting longer than 48 hours related to exercise) at each supervised exercise session.

Analysis of all other continuous secondary outcomes:

Descriptive statistics will be presented to summarise the distribution of baseline variables across study groups. The continuous baseline and post-acute and 12-week intervention variables will be reported with means and standard deviations if shown to be normally distributed (assessed via Shapiro-Wilks and visual inspection of Q-Q plots), otherwise they will be reported with medians and Interquartile Ranges. All categorical variables will be reported with frequencies and percentages.

Because this is a feasibility study, we will not be performing hypothesis testing on any measures. Instead, analysis will be mainly descriptive, we will provide pre-post mean

differences and 95% and 85% confidence intervals for within-group (exercise and standard care) and between-group (exercise vs. standard care) changes from baseline to post-acute exercise phase testing and baseline to post-12-week intervention phase.

Qualitative data analysis:

Qualitative data on patient satisfaction and acceptability: We will conduct qualitative semi-structured interviews with 15 patients in the intervention group to uncover their experience of the overall process, satisfaction with and acceptability of the exercise programme, and the match between activities and their needs and preferences. Patients will be selected for interviews regardless of their adherence to the exercise intervention Qualitative thematic data analysis of interview data will be conducted. Interviews will also be conducted with five participants randomly allocated to the control group with the aim of identifying needs for interventions that out intervention did not consider or cover.

Sample Size Determination

We are primarily interested in feasibility and acceptability, as well as outcome variability that will aid in the planning of a larger, sufficiently powered efficacy trial. There is a lack of consensus concerning the appropriate sample size for feasibility or pilot trials. Whitehead and colleagues (2016), however, recommend that for a main trial designed with 80% power and an alpha of 5%, a pilot trial sample size should be at least 10 participants per arm for standardised effects that are medium (standardised effect size = 0.5). However, we will allocate to intervention and standard care at a 2:1 ratio, to gain more data to inform the feasibility and acceptability of the active intervention, whilst still allowing for an estimate of the effect size and outcome variability which can be used to inform a sample size calculation in the subsequent confirmatory trial. Therefore, we will aim for a sample size of 30; 20 participants allocated to the intervention and 10 to the standard care. To account for 30% attrition, we will enrol 40 (27 to intervention and 13 to control) patients over a 10-month period.

Analysis populations

All patients randomised will be included in the analysis (intention-to-treat). We will also include a per protocol descriptive analysis of participants that achieved at least 90% adherence to the exercise intervention.

Decision points

Not applicable

Stopping rules

The protocol-specified stopping rules will be to stop the study if the number of reported serious adverse events exceed more than two per nine patients, three per 18 patients, or four per 27 patients (Scott 2018).

The Sponsor may suspend or prematurely terminate the study for significant reasons that must be documented (e.g., an unacceptable risk to participants or serious repeated deviations from the protocol/ regulations). If this occurs the Sponsor shall justify its decision in writing and will promptly inform any relevant parties (i.e., participants, investigators, recruitment site, REC, regulatory bodies).

The Level of Statistical Significance

We will not report p-values because we will include no formal hypothesis testing, however, we will provide pre-post mean differences, and 95% and 85% confidence intervals for all continuous measures.

Procedure for Accounting for Missing, Unused, and Spurious Data.

Reasons for all missing data will be recorded and reported. A complete case analysis will be used to compare baseline to post-acute and post-12-week intervention testing data descriptively.

Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any deviations from the original statistical plan will be described and justified in the final report.

Health Economics Analysis

Not applicable.