Demonstrating the (cost-)effectiveness of a personalized live-remote exercise intervention for cancer survivors using a super umbrella randomized controlled trial:
the LION-RCT

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The primary objective of the LION RCT is to assess the (cost-)effectiveness of a personalized, live-remote exercise intervention for cancer survivors on Health-Related Quality of Life (HRQOL) and the participants* main, self-reported side-effect....

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON56526

Source
ToetsingOnline

Brief title
LION-RCT

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer neoplasma

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Europese Unie en NHMRC

Intervention

Keyword: cancer survivors, exercise, live-remote, personalized

Outcome measures

Primary outcome

The primary endpoints of the LION RCT assessed at 12 weeks follow-up are:

- HRQOL: Summary score of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30

- A standardized symptom score per participant, based on their main side-effect defined at baseline:

o Physical fatigue (EORTC QLQ-FA12)

o Physical function (modified from EORTC QLQ-C30 physical function scale, i.e., the five QLQ-C30 physical function items and five items from the EORTC item bank that assess higher levels of physical functioning), anxiety and/or depressive symptoms (PHQ-ADS (Sum score PHQ-9 and GAD-7)), CIPN (EORTC QLQ-CIPN20)

Secondary outcome

Secondary endpoints are defined as:

* Additional Patient Reported Outcome Measures (PROMs):

o Other HRQOL domains of the EORTC QLQ-C30 (including physical functioning), except for the summary score.

o Fatigue (EORTC QLQ-FA12)

o Anxiety and/or depressive symptoms (PHQ-ADS)

o CIPN (EORTC QLQ-CIPN20 and 2 items of PRO-CTCAE)

o Sleep problems (PSQI)

o Pain (selected items from EORTC QLQ-SURV100)

o Cognitive problems (2 subscales from FACT-Cog)

o Work limitations (WLQ)

o Body image (BIS)

o Fear of recurrence (selected items from EORTC QLQ-SURV100)

o Habitual physical activity (Modified Godin)

* Physical fitness/performance/activity:

o Aerobic capacity (Maximal Short Exercise Capacity with the Steep Ramp Test &

Chester Step Test)

o Muscle strength: Upper body muscle strength (hand grip strength, hypothetical

1 repetition maximum (h1-RM)- chest press) and lower body muscle strength

(h1-RM leg press & 30 sec sit-to-stand test)

o Physical function (Timed Up & Go (TUG) test)

o Balance (Single Leg Stance test with open & closed eyes)

o Physical activity (activity tracker)

* Vital signs and anthropometrics

o Blood pressure

o Resting heart rate

o Anthropometrics

* Exercise-related biomarkers and blood cell counts

* Cost-effectiveness:

o Quality-Adjusted Life Years (QALYs) (EQ-5D-5L)

o Healthcare, patient and family costs (modified iMCQ)

o Productivity losses (modified iPCQ)

Safety endpoints:

- Exercise-related (serious) adverse events

Study description

Background summary

Many cancer patients suffer from long-term treatment-related side-effects like fatigue, low physical functioning, anxiety and/or depressive symptoms, and chemotherapy-induced peripheral neuropathy (CIPN). There is convincing evidence on the beneficial effects of general exercise interventions on these side-effects. However, studies to date generally fail to specifically screen for (long-term) side-effects at baseline and tailor the intervention to these specific side-effects, although larger exercise effects are observed in patients with a high symptom burden at baseline (e.g., with higher levels of fatigue). Larger effects of exercise are also observed for supervised exercise compared to unsupervised exercise. However, two of the most common barriers for attending and complying with supervised exercise are travel distance and time. An effective approach might be to provide live-remote supervision for exercise interventions. In this scenario, patients can receive guidance from a certified exercise specialist through a video-conferencing platform such as Zoom, while performing exercises within the comfort of their own homes. Currently, the effectiveness of live-remote exercise in cancer patients has not been established.

Study objective

The primary objective of the LION RCT is to assess the (cost-)effectiveness of a personalized, live-remote exercise intervention for cancer survivors on Health-Related Quality of Life (HRQOL) and the participants* main, self-reported side-effect. The four side-effects targeted in this study are: 1) fatigue, 2) perceived low physical functioning in daily life, 3) anxiety and/or

depressive symptoms, and 4) CIPN.

Study design

The LION RCT is a randomized controlled trial with two study arms: an exercise group (12 weeks) and a wait list control group. A super umbrella design will be used, allowing us to evaluate four exercise modalities (i.e., exercise modules based on participants* main side-effect) in a wide variety of cancer survivors.

Intervention

The intervention consists of three live-remote exercise sessions per week. Participants randomized to the exercise group receive the intervention after the baseline visit and the wait list control participants after the 12-week follow-up visit. A modular approach will be used to tailor the intervention to each participant*s specific main side-effect. Each participant will receive the same base module (twice a week) to address HRQOL and in addition one out of four specific modules (once a week) addressing their individual main side-effect. In addition to the live-remote training, participants will be provided with the LION app and an activity tracker (Fitbit) at the start of the intervention to support exercise beyond the supervised program, during holidays and after the end of the intervention. In addition to exercise, the intervention also has an educational component including information about general effects of exercise for cancer patients and why exercise is important for specific side-effects. We consider the provision of such education as an integral part of adequate exercise programming.

Study burden and risks

Burden
- Burden of the study comprises time-investment, i.e., 2-3 visits to the study center for measurements, completion of questionnaires at home (this takes approximately 20-45 minutes) , participation in a live-remote exercise program involving three hours of supervised exercise per week for 12 weeks. Additionally, participants will be asked to wear an activity tracker (Fitbit) during the study if feasible but at least one week after visit T0 and before visit T2, T4 and T5, during the training and online assessment sessions.

Risks
* As with any exercise, injuries can occur; to minimize the risk, the exercise program will be (live-remotely) supervised by a qualified exercise specialist. To ensure safety and optimal execution of the exercises, health issues or physical limitations that may hinder adherence to the standard exercise plan will be identified during the visit at the study center and communicated to the exercise trainer. In addition, a one-on-one intake session will be conducted live-remotely. The goal of this session is to check the technical connection,

assess the safety of the participant's home exercise environment, and go through the exercises. The exercise trainer will have the home address and an emergency contact for all participants.
* Following blood draws, a hematoma can occur.
* Incidental findings can arise during the different measurements (e.g., blood pressure measurement; assessment of depression and fresh blood analyses), which will be reported to participants and their treating physician when potentially clinically relevant.

Benefit
We expect that the exercise program will have a beneficial effect on the participants* health status.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

To be eligible to participate in this study, a subject must be:
o >= 18 years of age
o Diagnosed with any type of invasive or hematological cancer and completed their primary cancer treatment. Primary treatment, in this context, includes surgery, radiotherapy, and/or chemotherapy. For patients undergoing endocrine, targeted, or immunotherapy, their treatment must not be scheduled to be discontinued within the next 6 months.
o Have received systemic chemotherapy (or a stem cell transplantation in case of a hematological malignancy) as part of their primary cancer treatment with curative intent (or remission, without active disease and no expected active treatment within 1 year in case of hematological malignancies).
o No evidence of distant metastatic disease (in case of solid tumors; i.e., no diagnosis of metastatic disease in the regular clinical trajectory)
o ECOG (Eastern Cooperative Oncology Group) performance status <= 2
o Presence of at least one of the following side-effects: fatigue (measured using EORTC QLQ-C30 fatigue symptom scale, score >39), perceived low physical functioning in daily life (measured using EORTC QLQ-C30 physical functioning scale, score <83), anxiety or depressive symptoms (measured using PHQ-ADS > 20), and/or CIPN (measured using 2 PRO-CTCAE items, score >0) for patients who received neurotoxic chemotherapy. Cut-off values are based on established thresholds.
o Access to good quality and stable internet connection to access the live-remote training sessions.
o Able and willing to perform the exercise program and wear the activity tracker at least one week after T0 and around T2, T4, and T5 measurements and during training and online assessment sessions.
o Able to read, speak and understand Dutch (for the other countries: their main language)

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
o Too physically active (i.e., >150 minutes/week of self-reported moderate-to-vigorous intensity leisure and sports activities; this threshold has also been used in other exercise RCTs and fits activity levels of all participating countries)or participation in an exercise program comparable to the LION exercise program.
o Did receive chemotherapy as part of treatment for a previous diagnosis.
o Following or planned to follow a structural psychological intervention during the intervention period, i.e., cognitive behavioral therapy, or unstable on psychotropic medication

o Participated in structured exercise intervention comparable to the LION exercise program during cancer treatment.
o Inability to complete the testing or training sessions or any other contraindications for exercise as determined by the treating physician, including:
o Severe neurologic or cardiac impairment according to ACSM criteria
o Uncontrolled severe respiratory insufficiency or dependence on oxygen suppletion in rest or during exercise
o Uncontrolled pain

o Any circumstances that would impede ability to give informed consent or adherence to study requirements as determined by the treating physician
o More than 1 week not able to attend training sessions during the LION intervention period.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-02-2024
Enrollment:	88
Type:	Actual

Ethics review

Approved WMO

Date:	18-01-2024
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	13-05-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-01-2025
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85029.041.23