



I JORNADA SEOM EJERCICIO FÍSICO Y CÁNCER

17 DE JUNIO DE 2024

Meeting Place. Paseo de la Castellana, 81. Madrid

**Modelos clínicos de Investigación en ejercicio
Físico y Cáncer**

Ander Urruticoechea

Unidad de Gestión del Cáncer de Gipuzkoa: HU Donostia-Onkologikoa-Osakidetza

SEOM
Sociedad Española
de Oncología Médica

Fundación
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GRUPO DE TRABAJO SEOM DE
ejercicio y
CÁNCER

GE'icam
investigación en
cáncer de mama



Disclosure Information

- Travel arrangements to meetings:

Gilead, AZ-Daychii Sankyo, Novartis



#EjercicioContraelCáncer



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International guidelines

Exercise is beneficial during and after cancer treatment and hence recommended.

American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control

ALPNA V. PATE¹, CHRISTINE M. FRIEDENBERG², STEPHEN J. MCKERR³, SANDRA C. HAYES⁴, DALE K. SEVIER⁵,
KURTIN L. CAMPELL⁶, KIRBY WINTERSTONE⁷, LYNN H. GERBER⁸, STEPHANIE H. GEORGE⁹,
DANIEL FULTON¹⁰, KRISTAL OLSINGER¹¹, C. STEPHEN BRIGGS¹², ROSA WU¹³, KATHRYN A. SCHMITZ¹⁴,
and CHARLES E. MATTHEWS¹⁵

MEDICINE & SCIENCE IN SPORTS & EXERCISE 2019

Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline

Jennifer A. Ligibel, MD¹, Karl Holche, ScD², Anne M. Mac, PhD³, Steven K. Eckert, MD, PhD⁴, Wendy Deming-Hartnett, PhD, RD⁵,
Susan C. Ekkehardt, MD, MS⁶, Melissa L. Irwin, PhD, MPH⁷, Shireen Lata⁸, Sarah Hunsford, BA⁹, Timothy F. Mackel, PhD, MPH¹⁰,
Jeffrey A. Meyerowitz, MD, MPH¹¹, Cynthia A. Thomson, PhD, RD¹², William A. Pines, MD, MPH¹³, and Catherine M. Alfano, PhD¹⁴

JOURNAL CLINICAL ONCOLOGY 2022

Outcomes

Strong evidence

- Anxiety
- Depressive symptoms
- Fatigue
- Quality of life
- Physical functioning
- Lymphedema

Moderate evidence

- Sleep
- Bone health

Insufficient evidence

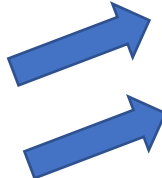
- Cardiotoxicity
- CIPN (neuropathy)
- Cognitive functioning
- Risk of falls
- Nausea
- Pain
- Sexual functioning
- Treatment adherence

Cancer types

Mainly:

- Breast cancer
- Prostate cancer

- Other cancer types
- Advanced cancers



Focus Your Search
(all filters optional)

Condition/disease ⓘ
Cancer

Other terms ⓘ
Physical Activity

Intervention/treatment ⓘ
[Empty field]

Location
Search by address, city, state, or country and select from the dropdown list
[Empty field]

Study Status ⓘ

Looking for participants

- Not yet recruiting (703)
- Recruiting (3,335)

No longer looking for participants

- Active, not recruiting (1,422)

[Clear Filters \(2\)](#) [Apply Filters](#)

Search Results

Viewing 1-10 out of 16.402 studies

[Card View](#) [Table View](#)

Showing results for: **Cancer** | Other terms: **Physical Activity**

[+ Synonyms of conditions or disease \(22\)](#)

[None Selected](#) [Download](#) [Bookmark](#) [RSS](#)

NOT YET RECRUITING

NCT05981170

Rurality Adapted Physical Activity Sport Health

Conditions

[Brain Tumour](#) [Metastatic Cancer](#)

Locations

[Angers, France](#)

COMPLETED

NCT03212079

Physical Activities by Technology Help (PATH)

Conditions

[Breast Cancer](#) [Cervical Cancer](#) [Colorectal Cancer](#) [Lung Cancer](#) [Show 2 more conditions](#)

PREFERABLE I

Effects of a structured and individualized exercise program on fatigue and health-related quality of life in patients with metastatic breast cancer: the multinational randomized controlled PREFERABLE-EFFECT study

Authors: Anne May, Anouk Hiensch, Johanna Deppenbusch, Martina Schmidt, Evelyn Monninkhof, Mireia Pelaez, Dorothea Clauss, Philipp Zimmer, Jon Belloso, Mark Trevaskis, Helene Rundqvist, Joachim Wiskemann, Jana Müller, Carlo Fremd, Renske Altena, Joanna Kufel-Grabowska, Rhode Bijlsma, Lobke van Leeuwen-Snoeks, Daan ten Bokkel-Huinink, Gabe Sonke, Bruce Mann, Prudence Francis, Gary Richardson, Wolfram Malter, Elsken van der Wall, Neil Aaronson, Elzbieta Senkus, Ander Urruticoechea, Eva Zopf, Wilhelm Bloch, Martijn Stuiver, Yvonne Wengström, Karen Steindorf

Manuscript in press: Nature Medicine

Acknowledgements

Anouk Hiensch, Johanna Depenbusch, Martina Schmidt, Evelyn Monnikhof, Mireia Pelaez, Dorothea Clauss, Philipp Zimmer, Jon Beloso, Mark Trevaskis, Helene Rundqvist, Joachim Wiskemann, Jana Müller, Carlo Fremd, Renske Altena, Joanna Kufel-Grabowska, Rhode Bijlsma, Lobke van Leeuwen-Snoeks, Daan ten Bokkel-Huinink, Gabe Sonke, Bruce Mann, Prudence Francis, Gary Richardson, Wolfram Malter, Elsen van der Wall, Neil Aaronson, Elzbieta Senkus, Ander Urruticoechea, Eva Zopf, Wilhelm Bloch, Martijn Stuiver, Yvonne Wengström, Karen Steindorf



Thanks to all **participating patients**;
all **treating physicians and nurses** in participating hospitals;
physiotherapists and exercise trainers.



Participating centers



In collaboration with



Funded by



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825677; and the Australian Government (2018/GNT1170698).

Introduction – effects of exercise during cancer treatment

Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline

Jennifer A. Ligibel, MD¹; Kari Bohlke, ScD²; Anne M. May, PhD³; Steven K. Clinton, MD, PhD⁴; Wendy Demark-Wahnefried, PhD, RD⁵; Susan C. Gilchrist, MD, MS⁶; Melinda L. Irwin, PhD, MPH⁷; Michele Late⁸; Sami Mansfield, BA⁹; Timothy F. Marshall, PhD, MS¹⁰; Jeffrey A. Meyerhardt, MD, MPH¹; Cynthia A. Thomson, PhD, RD¹¹; William A. Wood, MD, MPH¹²; and Catherine M. Alfano, PhD¹³

J Clin Oncol 40:2491-2507. © 2022 by American Society of Clinical Oncology

RESULTS - Exercise during **adjuvant** cancer treatment leads to improvements in cardiorespiratory fitness, strength, fatigue, and other patient-reported outcomes.

RECOMMENDATION - Oncology providers should recommend regular aerobic and resistance exercise during active treatment **with curative intent**.

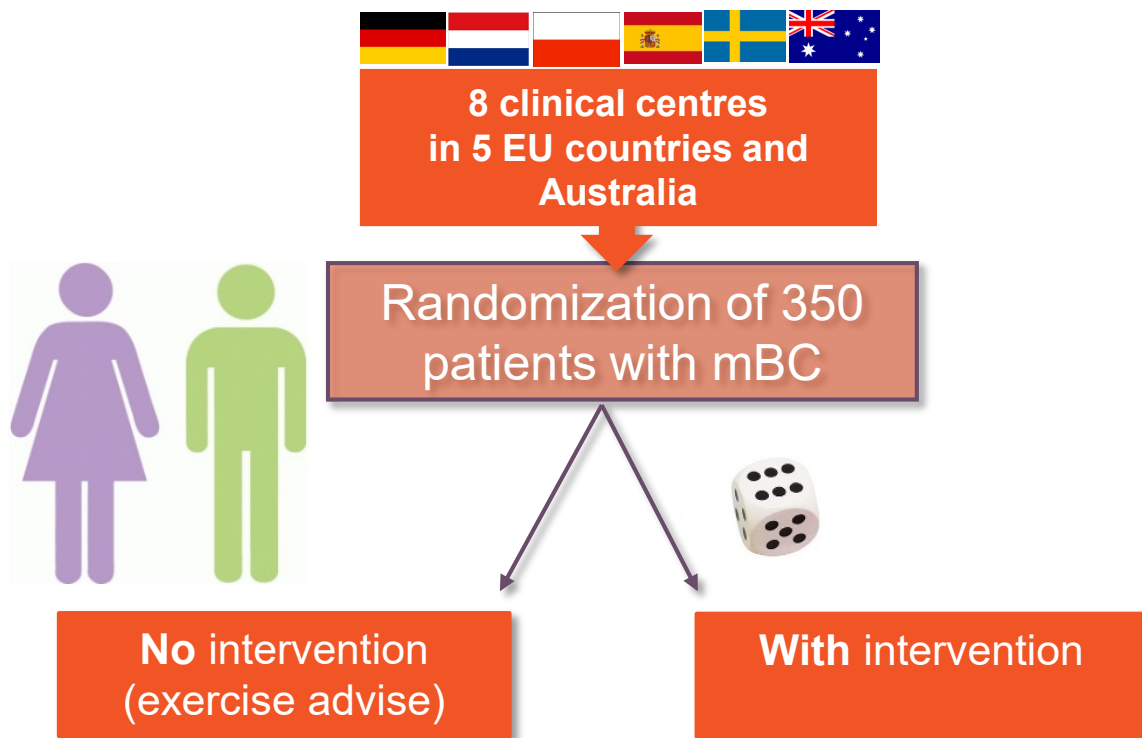
FUTURE RESEARCH - Studies are needed in ... **those with metastatic disease**.

Aim – PREFERABLE-EFFECT trial

To investigate the effects of **supervised** and individualized **exercise** in patients with **metastatic breast cancer** on **fatigue** and **quality of life**.



Methods



Inclusion criteria:

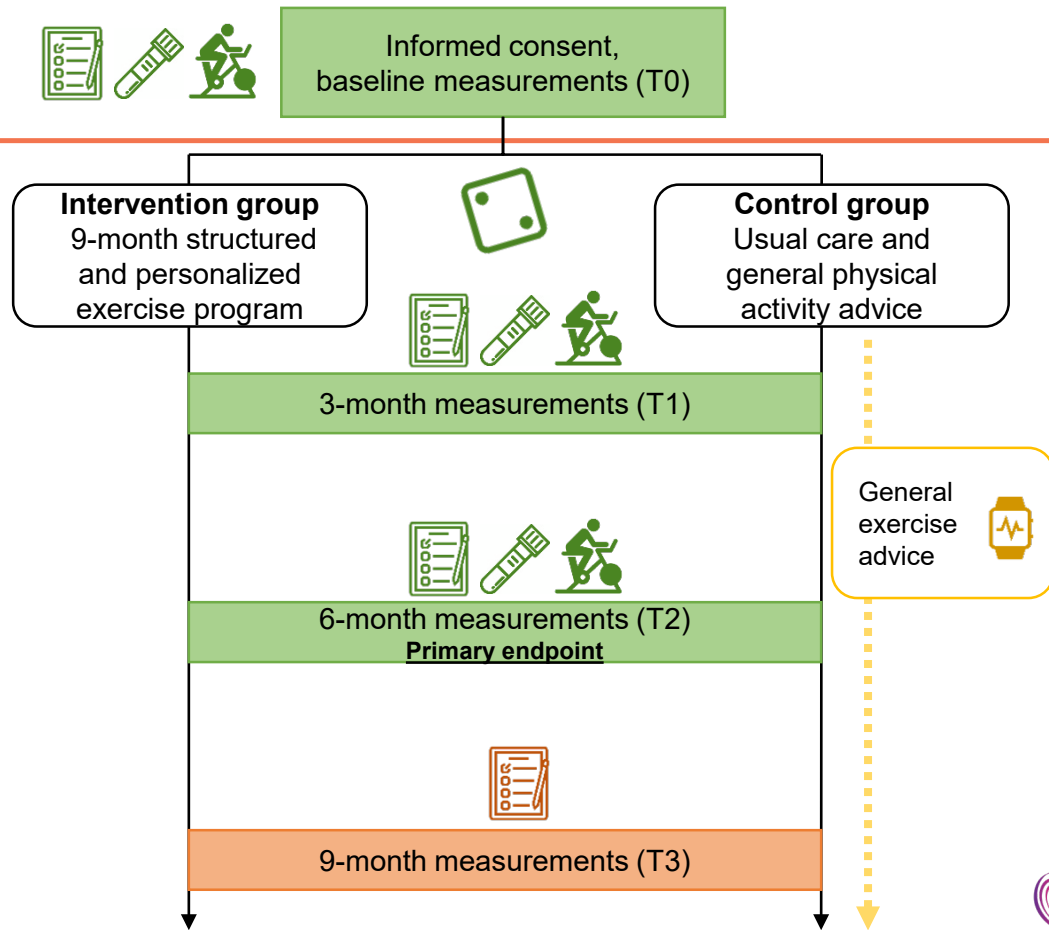
- Age ≥ 18 years
- Diagnosis of breast cancer stage IV
- ECOG performance status ≤ 2
- Life expectancy of ≥ 6 months

Exclusion criteria:

- Contraindication for exercise
- Unstable bone metastases
- Too physically active (>210 min/wk)



Methods



Methods



Informed consent,
baseline measurements (T0)

Intervention group
9-month structured
and personalized
exercise program

Control group
Usual care and
general physical
activity advice

3-month measurements (T1)

6-month measurements (T2)
Primary endpoint

9-month measurements (T3)

Supervised exercise:
2x p.w. 60 min



Exercise
advice



Supervised exercise:
1x p.w. 60 min
Unsupervised exercise:
1x p.w. 60 min

General
exercise
advice



Aerobic training
moderate-intensity & high-intensity
interval training
Resistance Training
major lower and upper body
muscles
Balance training



Methods - Outcomes

Primary endpoints:

- Cancer-related **physical fatigue**
- Health-related **QoL**

Secondary endpoints include:

- Pain, breast cancer specific symptoms, anxiety, depression
- Polyneuropathy, sleep
- Treatment related toxicities
- **Physical fitness**/performance, body composition
- Biomarkers
- Physical activity
- QALYs and direct and indirect costs



- EORTC-FA-12
- EORTC-QLQ-30 **summary** score

Trial successful if either or both are statistically significant.*




- Steep ramp test (maximal short exercise capacity (MSEC))


*At 6-month post baseline, using mixed effect models adjusted for baseline and stratification factors (Bonferroni correction).





Results – Baseline characteristics


Intervention group (n=178)

 Age (years)
54.9 ± 11.6


 Female
99.4%


 Higher education degree
73.6%


 Married/living together
68.0%


 BMI
25.9 ± 5.1


Control group (n=179)

 Age (years)
55.9 ± 10.7

 Female
99.4%

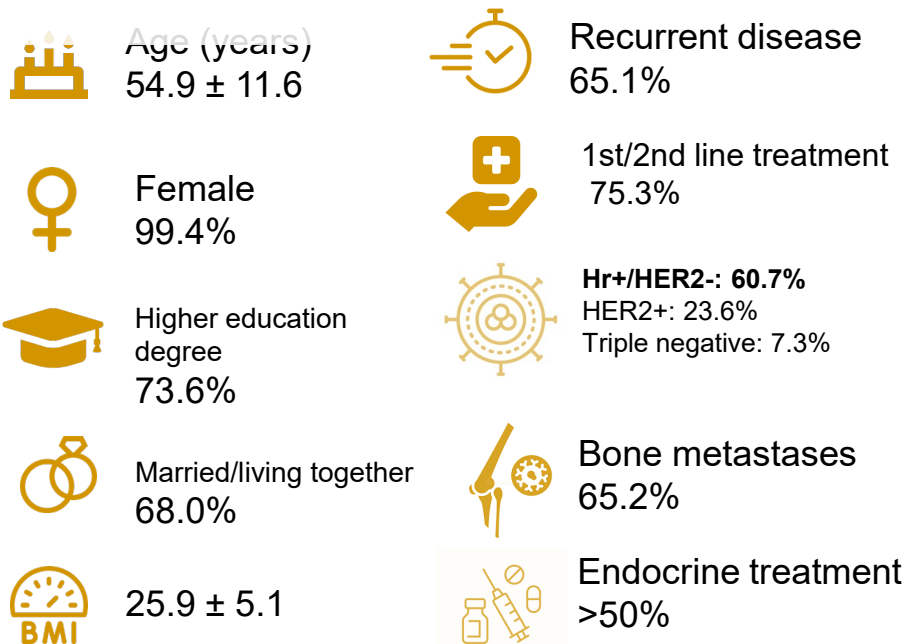
 Higher education degree
76.0%

 Married/living together
65.4%

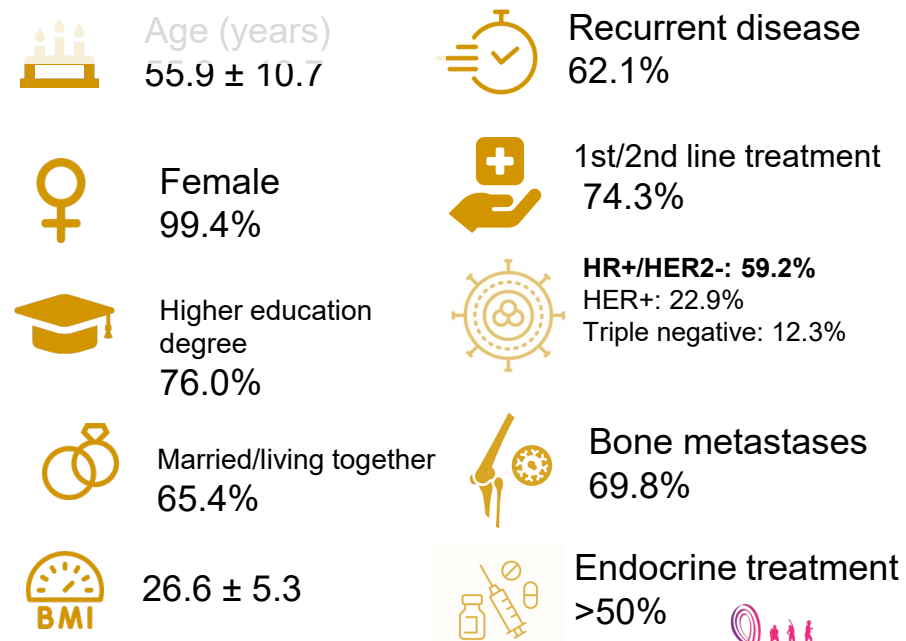
 BMI
26.6 ± 5.3

Results – Baseline characteristics

Intervention group (n=178)



Control group (n=179)

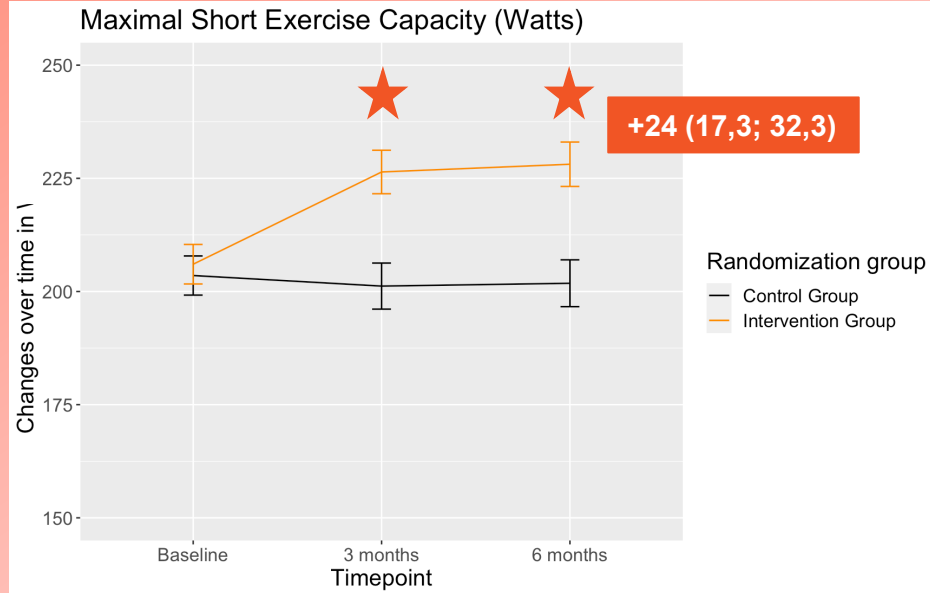


Results – Attendance, SAEs & physical fitness outcome



Median **attendance**
[IQR] = 77% [48-92]

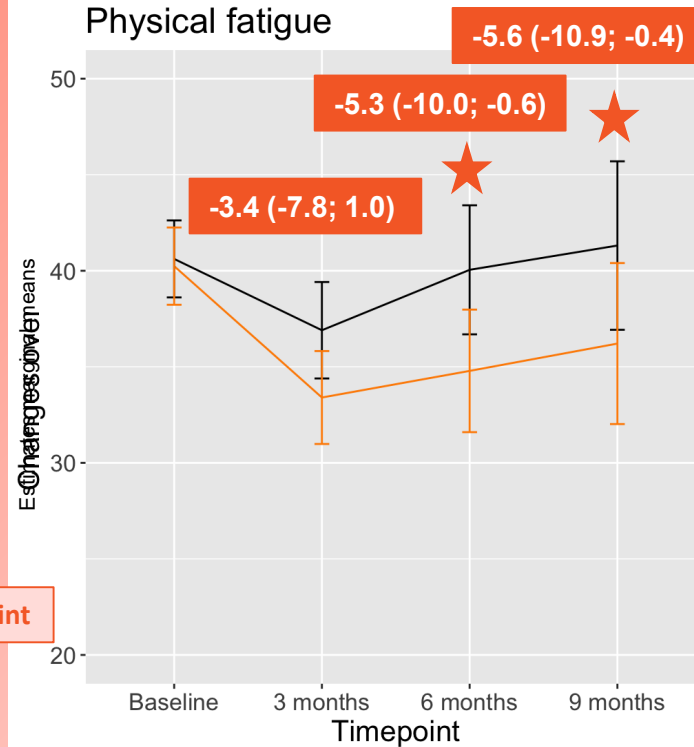
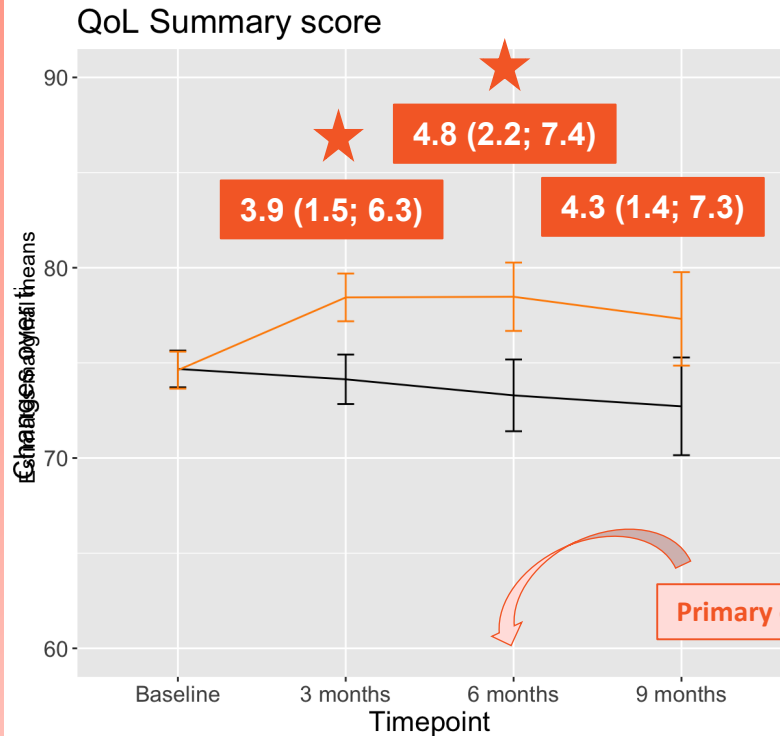
6-month post-BL:
18% **discontinuation**
• 44% due to death



Two SAEs: 1 wrist fracture and 1 sacral stress fracture, none related to bone metastases.



Results – Primary outcomes



Randomization group

— Control Group
— Intervention Group

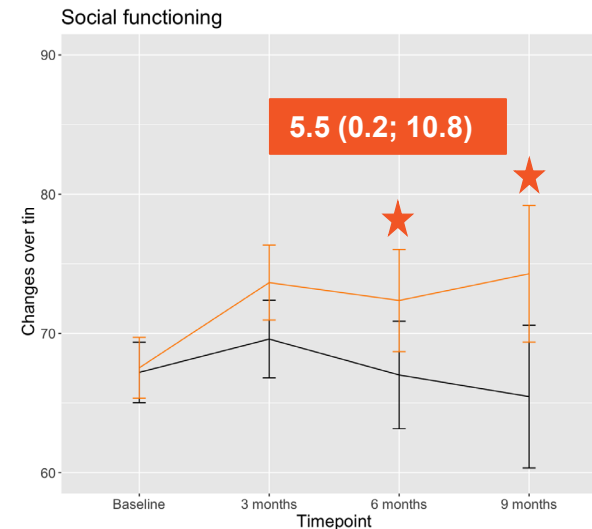
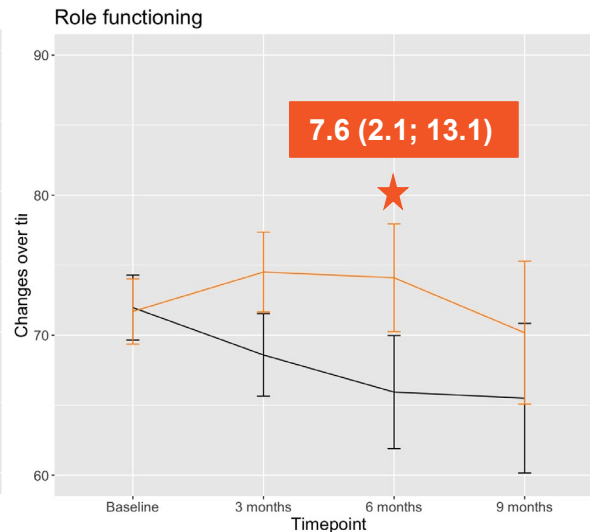
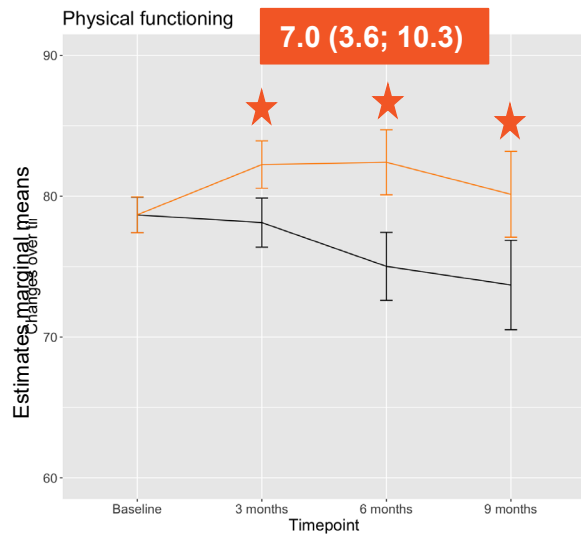
★ Significant between-group differences



Results – QoL functional scales

Randomization group

- Control Group
- Intervention Group



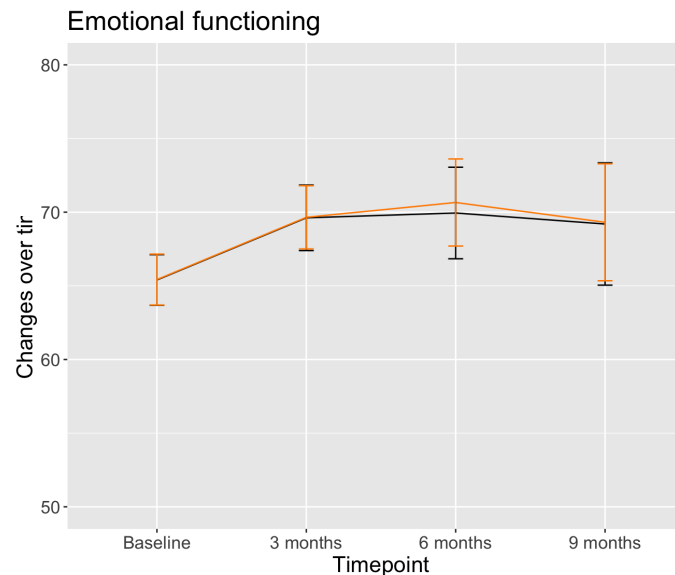
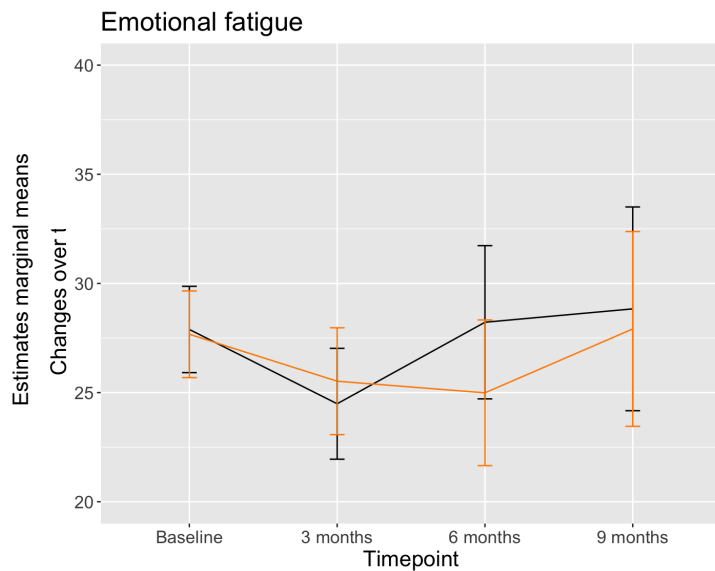
★ Significant between-group differences



Results – Emotional fatigue and functioning

Randomization group

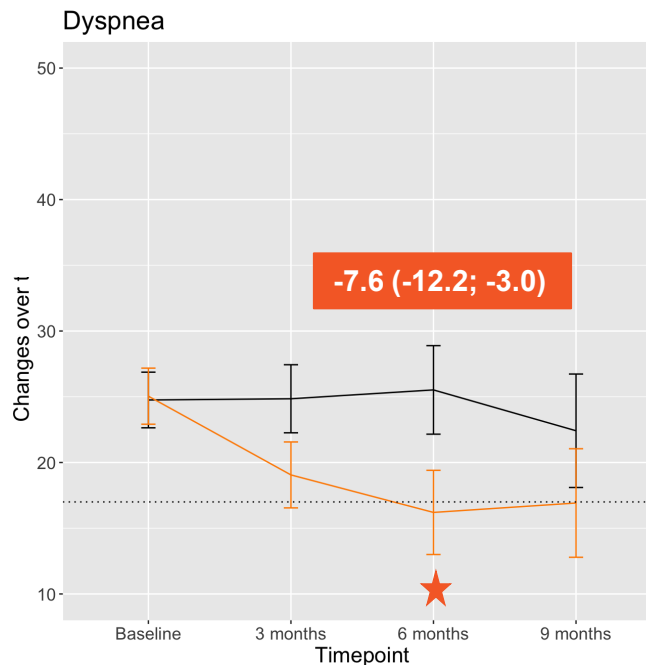
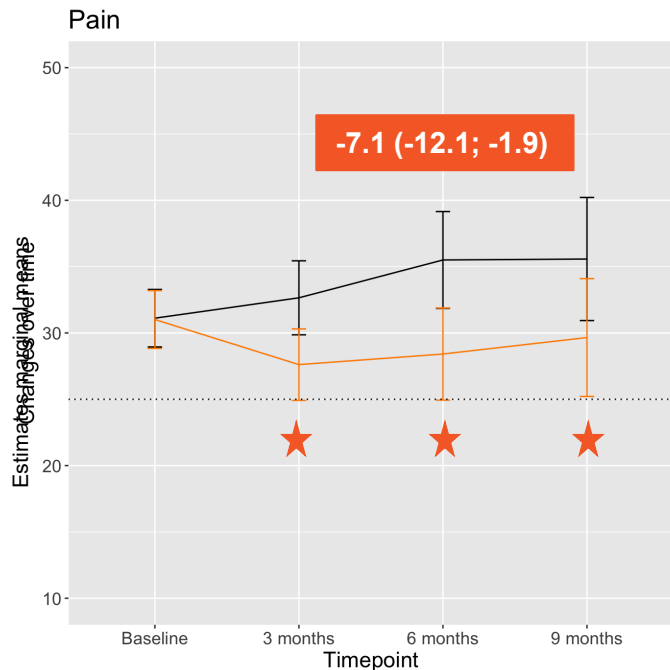
- Control Group
- Intervention Group



Results – Pain and dyspnea

Randomization group

- Control Group
- Intervention Group



PREFERABLE-PERSPECTIVE
(questionnaire n=420):

Concerns that **pain** and **fatigue** worsens while exercising

(Sweegers et al. Sup. Care Can. 2023)

58%

% Scoring above clinical important threshold at baseline*

57%

Pain

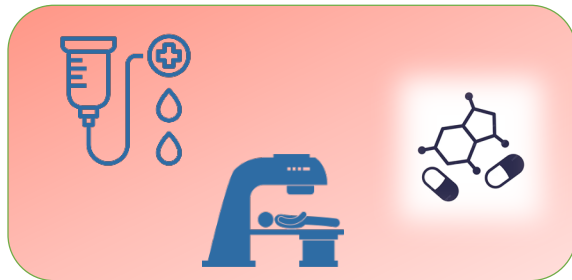
* Giesinger et al. J Clin Epidemiol. 2020

Dyspnea



Conclusions

- A supervised resistance and aerobic exercise intervention resulted in beneficial effects on fatigue, HRQoL, and other clinically relevant outcomes of patients with mBC.
- We recommend supervised exercise as part of supportive care regimens during palliative treatment.





PREFERABLE II

The effects of live-remote exercise in patients with complaints after cancer treatment

INTRODUCTION TO THE PREFERABLE II AND OUTCOMES

Prof. Dr. Anne May



PREFERABLE partners



Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union. Neither the European Union nor the granting authority can be held responsible for them. The contents of the published material are solely the responsibility of the authors and do not reflect the views of NHMRC.



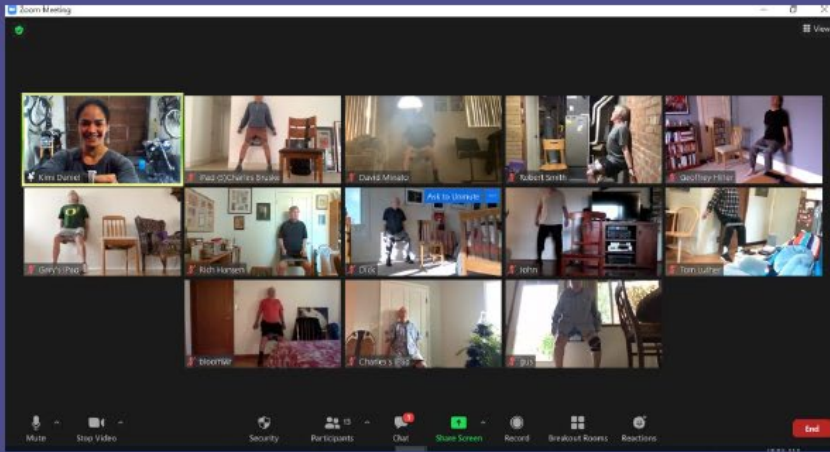
Funded by European Union



Co-funded by



PREFERABLE II – effects of live-remote exercise



- Telemedicine: One broadcast center per country
- Upscaling to other countries by establishing a broadcast center there and train a limited number of trainers

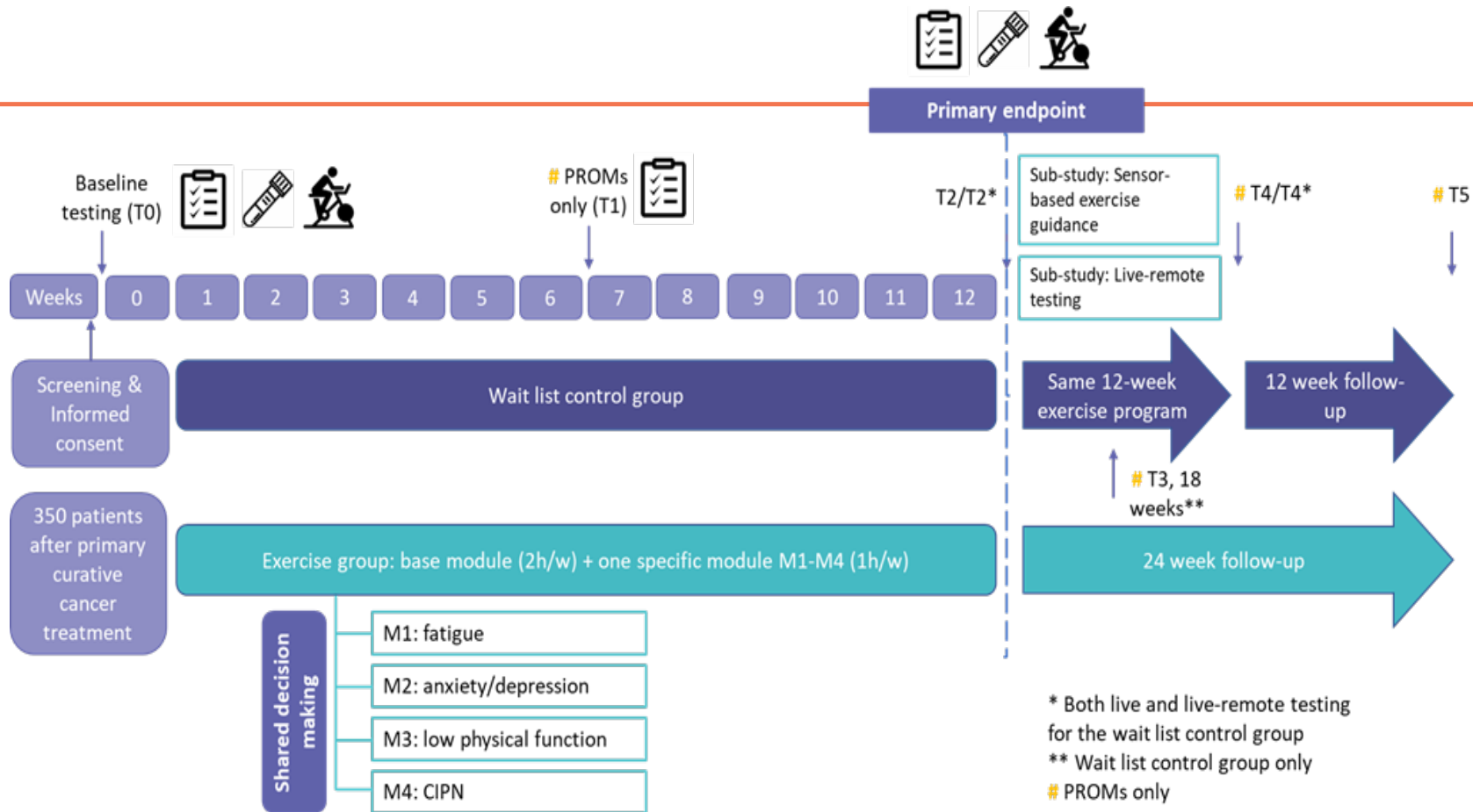
LION RCT

The primary objective of the LION RCT is to assess the (cost-)effectiveness of a personalized, **live-remote** exercise intervention for cancer survivors on

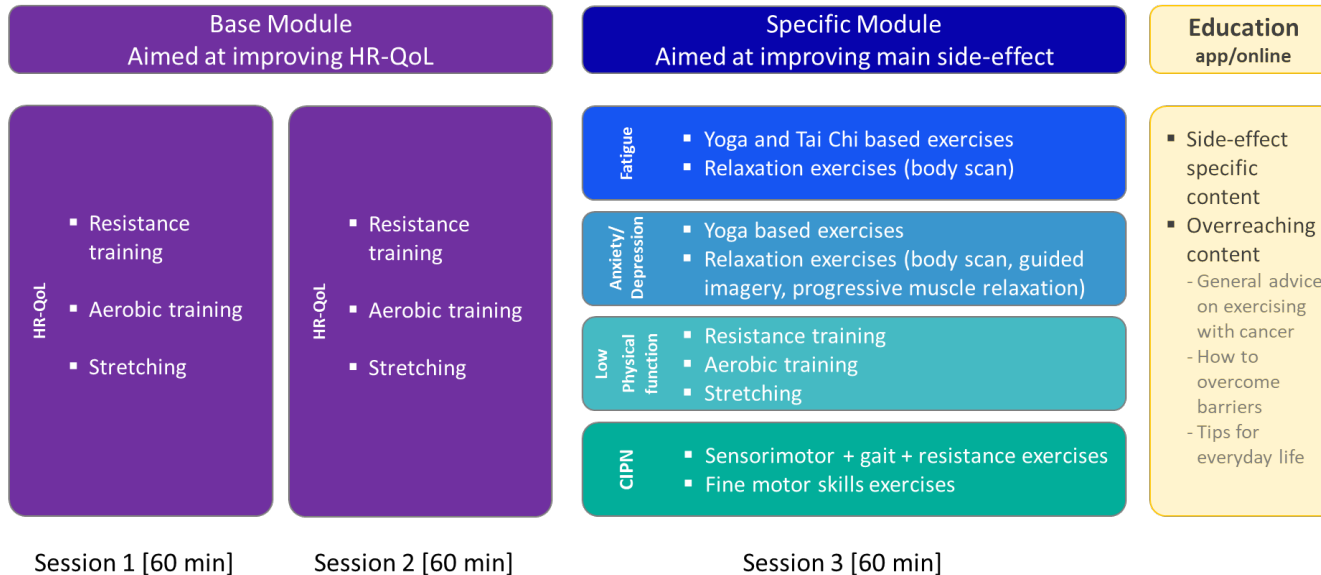
1) **HRQOL** and

2) the participants' **main, self-reported side-effect**. The four side-effects targeted in this study are:

- fatigue,
- perceived low physical functioning in daily life,
- anxiety and/or depressive symptoms,
- and **Cancer Induced Peripheral Neuropathy**.



Live remote supervision for all modules from cancer exercise specialists via national broadcast centers





Food for thought

1

Diseños de
Ensayo



2

Focos de
Investigación

RESEARCH

Open Access



The Trial within Cohorts (TwiCs) study design in oncology: experience and methodological reflections

Rob Kessels¹, Anne M. May^{2*}, Miriam Koopman³ and Kit C. B. Roes⁴

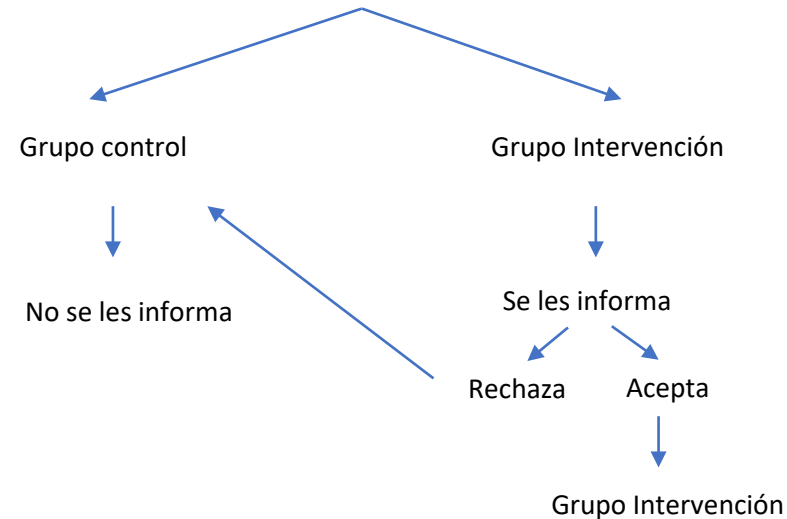
Abstract

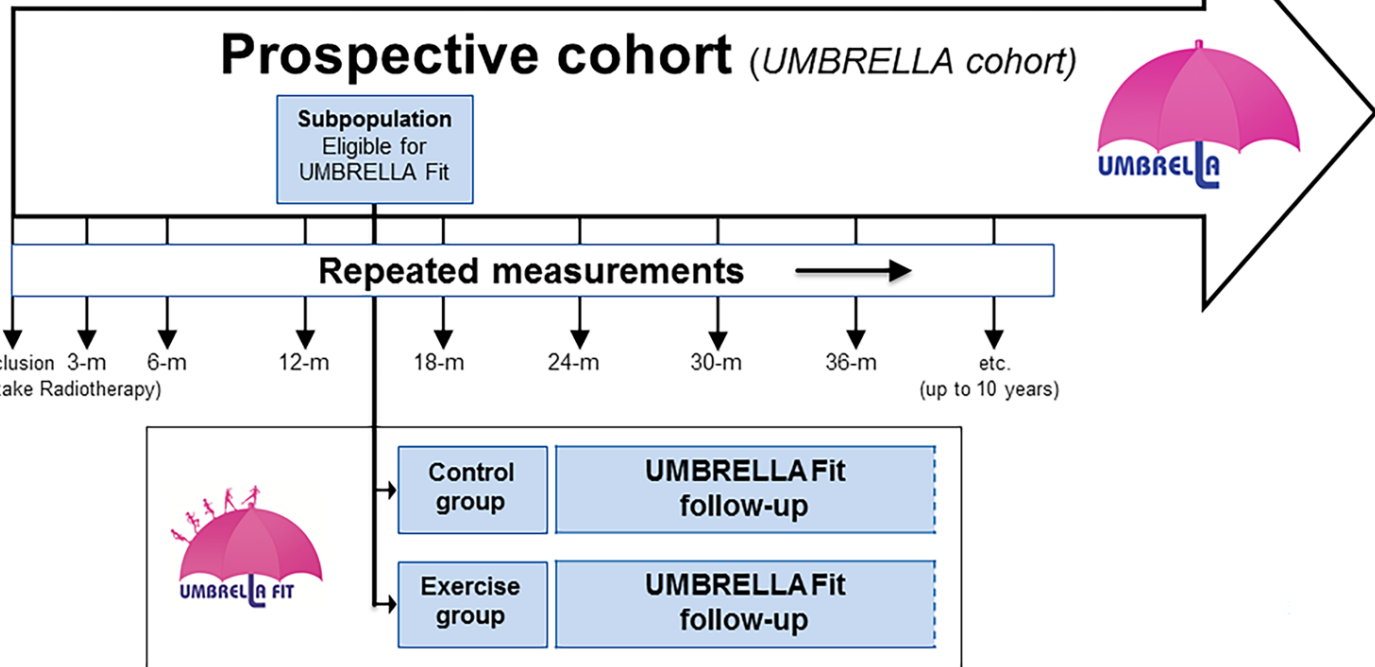
A Trial within Cohorts (TwiCs) study design is a trial design that uses the infrastructure of an observational cohort study to initiate a randomized trial. Upon cohort enrollment, the participants provide consent for being randomized in future studies without being informed. Once a new treatment is available, eligible cohort participants are randomly assigned to the treatment or standard of care. Patients randomized to the treatment arm are offered the new treatment, which they can choose to refuse. Patients who refuse will receive standard of care instead. Patients randomized to the standard of care arm receive no information about the trial and continue receiving standard of care as part of the cohort study. Standard cohort measures are used for outcome comparisons. The TwiCs study design aims to overcome some issues encountered in standard Randomized Controlled Trials (RCTs). An example of an issue in standard RCTs is the slow patient accrual. A TwiCs study aims to improve this by selecting patients using a cohort and only offering the intervention to patients in the intervention arm. In oncology, the TwiCs study design has gained increasing interest during the last decade. Despite its potential advantages over RCTs, the TwiCs study design has several methodological challenges that need careful consideration when planning a TwiCs study. In this article, we focus on these challenges and reflect on them using experiences from TwiCs studies initiated in oncology. Important methodological challenges that are discussed are the timing of randomization, the issue of non-compliance (refusal) after randomization in the intervention arm, and the definition of the intention-to-treat effect in a TwiCs study and how this effect is related to its counterpart in standard RCTs.

Keywords Trials within Cohorts, TwiCs, Cohort multiple randomized controlled trial, Oncology, Non-compliance, Efficacy estimand

Al abrir la cohorte el paciente ingresa dando consentimiento para ser aleatorizado en estudios sin ser informado si no es necesario

Al abrir el estudio los pacientes son Aleatorizados

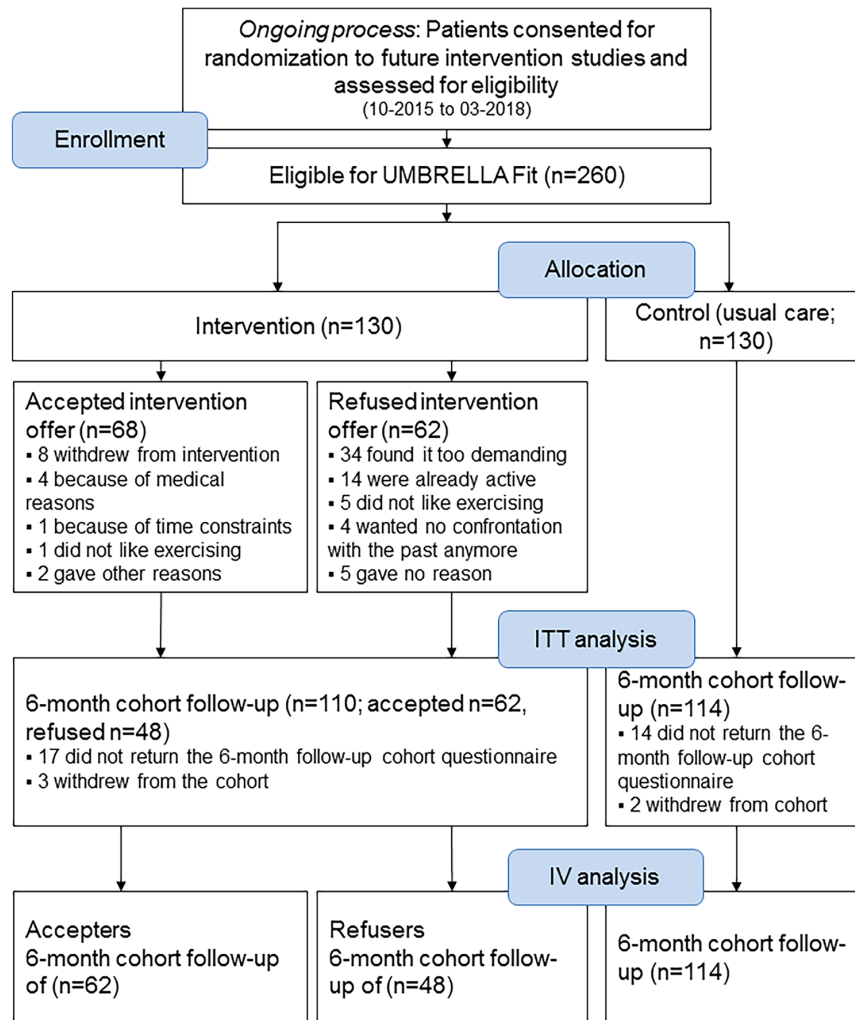




Umbrella Fit Trial
Gal et al. Br Ca Res Treat 2021

 #EjercicioContraelCáncer

Umbrella Fit Trial
Gal et al. Br Ca Res Treat 2021





Food for thought

1

Diseños de
Ensayo

2

Focos de
Investigación



¿> 16.000 ensayos?



Estudios de
Implementación /
factibilidad
en nuestros sistemas
sanitarios / sociales



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GRACIAS POR
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