



Effects of Exercise in Patients with Metastatic Breast Cancer: Results of the PREFERABLE-EFFECT Study

Prof. Dr. Anne May



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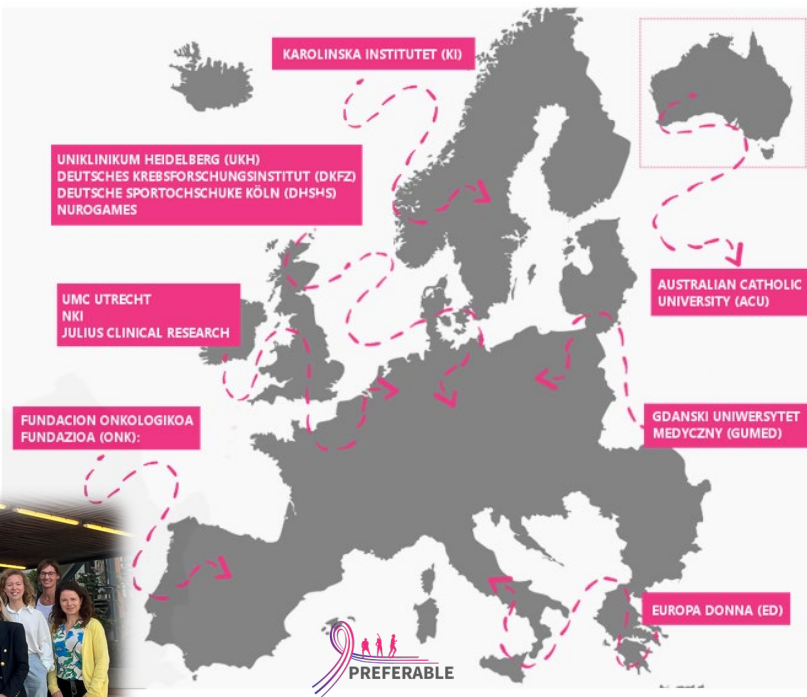


Disclosure

I have no actual or potential conflict of interest in relation to this presentation.

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

Participating centers



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Research for a Life without Cancer



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@PREFERABLE_MBC

<https://www.h2020preferable.eu/>

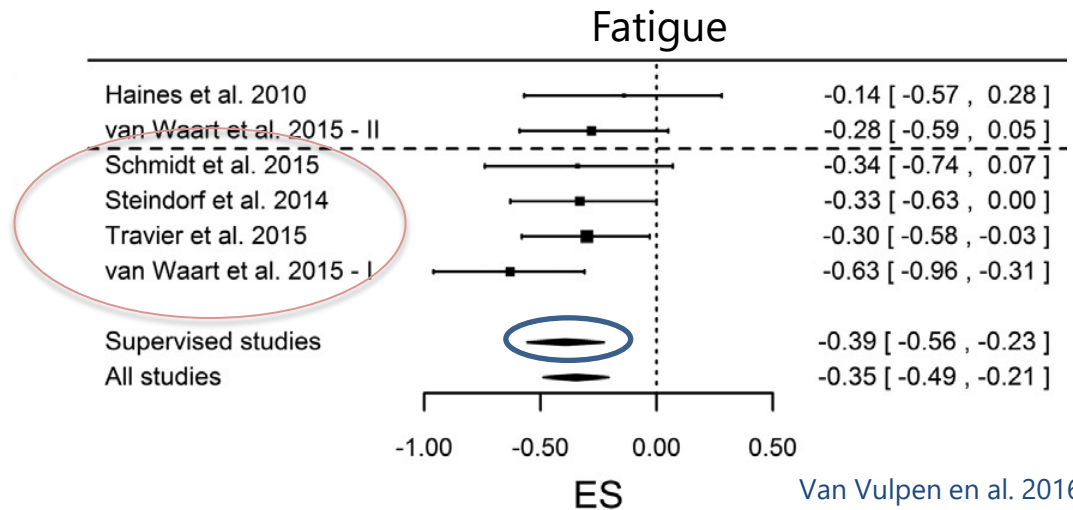
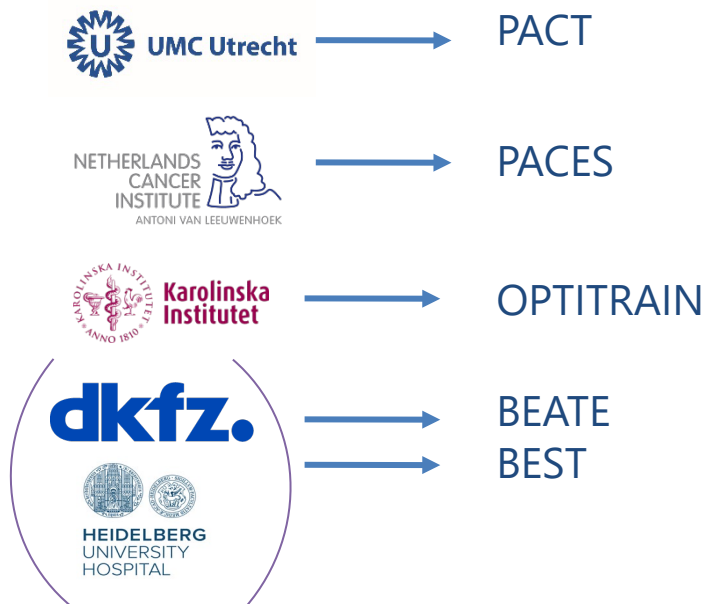
Aim PREFERABLE- EFFECT trial

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



Why did we start PREFERABLE?

Based on promising evidence regarding **supervised exercise** in early stage breast cancer:



Exercise-oncology guidelines

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

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2019
Update Cancer
exercise
recommen-
dations (ACSM
int. roundtable
2018; Campbell
et al. MSSE 2019)

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**.

PREFERABLE-EFFECT trial

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



**8 clinical centres
in 5 EU countries and
Australia**

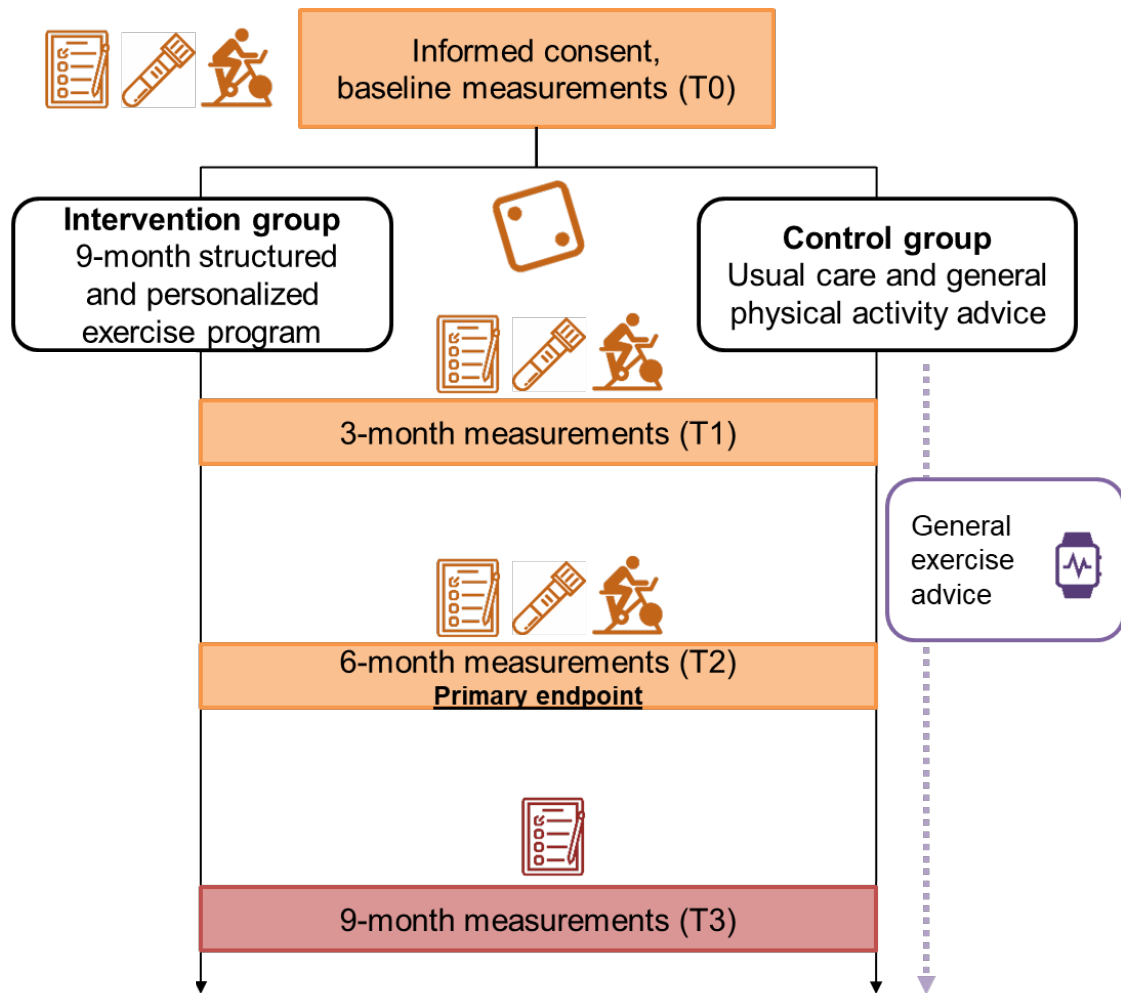
Inclusion criteria:

- Age ≥ 18 years
- Diagnosis of breast cancer stage IV
- Life expectancy of ≥ 6 months

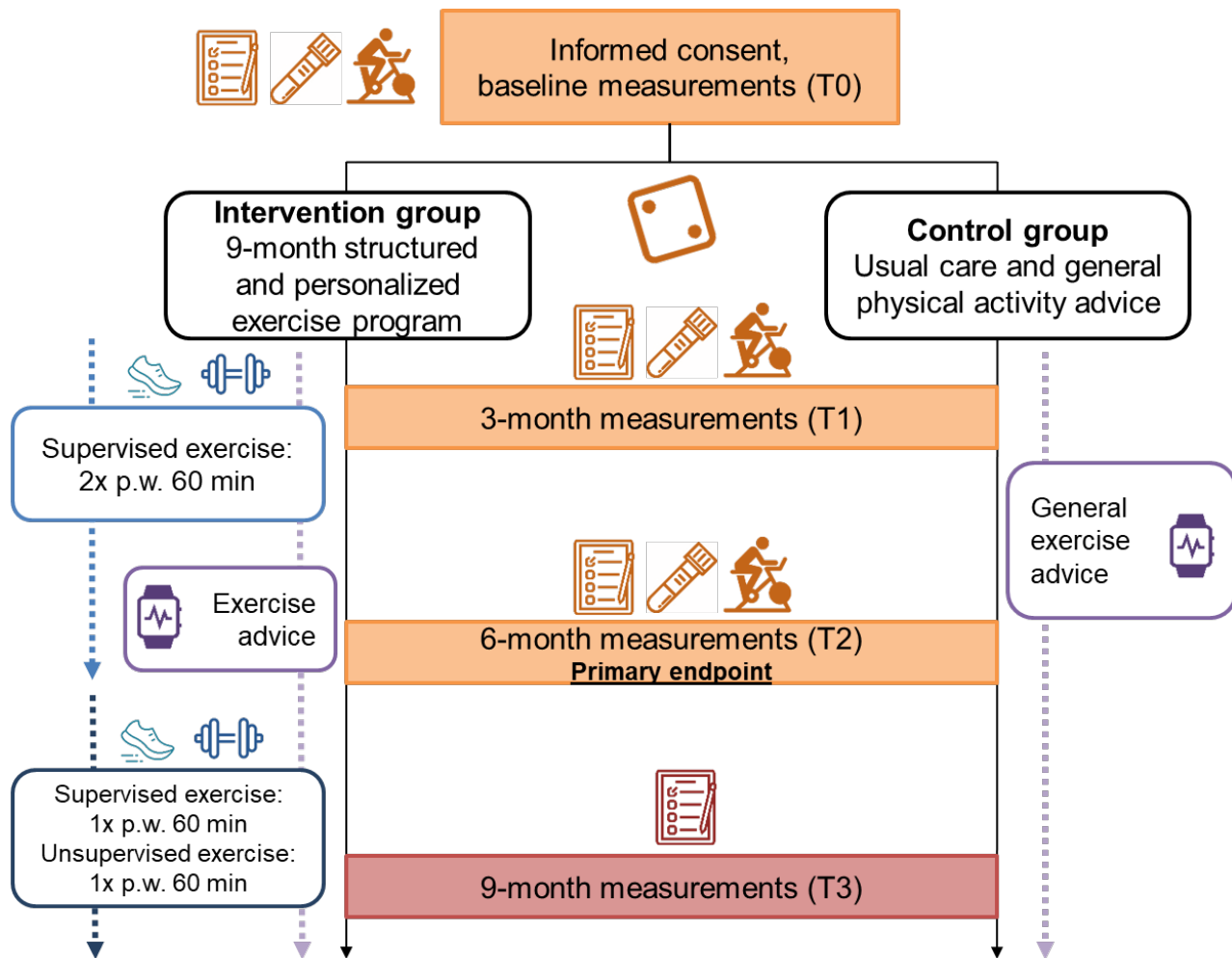
Exclusion criteria:

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

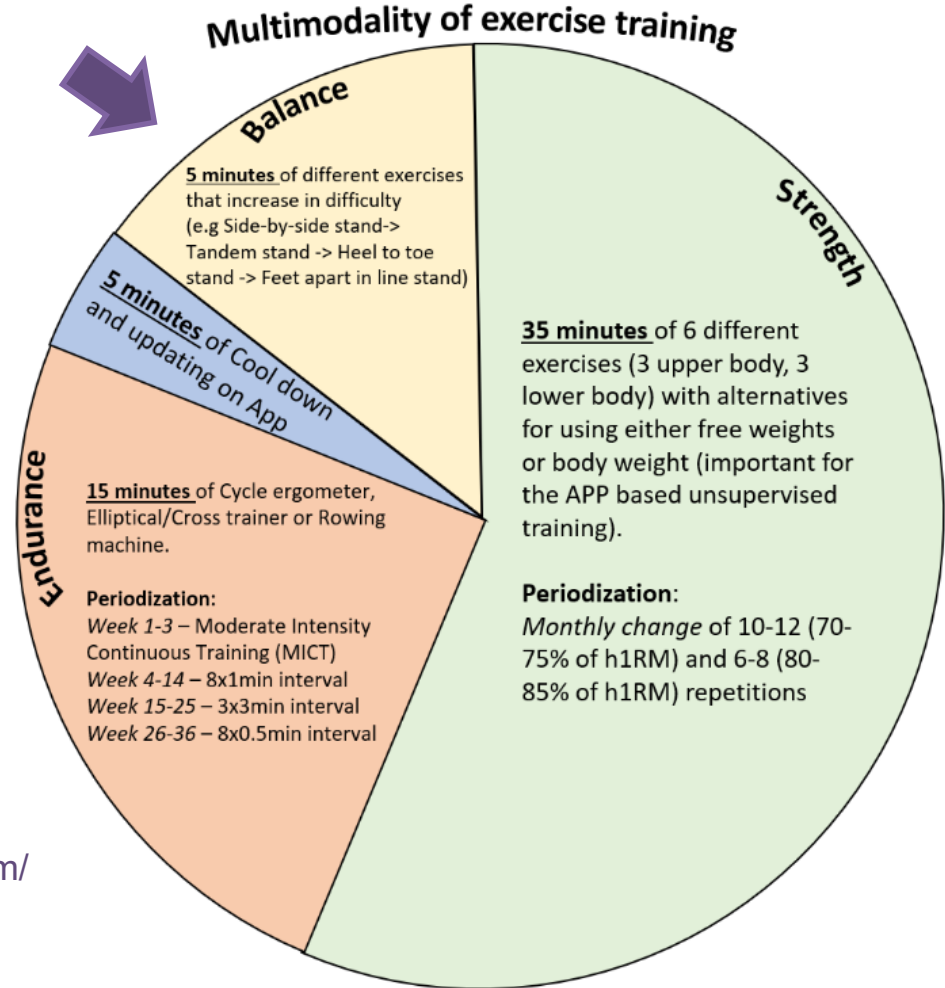
Methods



Methods



Methods



Download the exercise program:

<https://www.h2020preferable.eu/exercise-program/>

Adaptations to the exercise program based on location of metastases in PREFERABLE-EFFECT

Metastases site	Resistance exercise ^a			Aerobic exercise		Flexibility
	Upper	Trunk	Lower	WB	NWB	Static
Pelvis	✓	✓	✓ ^c		✓	✓
Axial skeleton (lumbar)	✓		✓		✓	✓ ^d
Axial Skeleton (thoracic/ribs)	✓ ^b		✓	✓	✓	✓ ^d
Proximal humerus		✓ ^b	✓	✓	✓	✓ ^b
Proximal femur	✓	✓	✓ ^c		✓	✓
All regions	✓ ^b		✓ ^c		✓	✓ ^d

This table is adapted from Galvão et al. (2011) [14]

^a Resistance exercises that load the affected region can be either omitted according this table or can be performed using a “start low, go slow” approach, depending on patient characteristics and the experience of the involved trainer. According to this approach, participants with bone metastases should start with low weights and more repetitions and increase weights gradually over time up to 10–12 repetitions if possible. Higher intensities (i.e., 6–8 repetitions with 80–85% of h1RM) should be avoided. Weights will be reduced if participants report pain during a resistance exercise or experience an increase in pain or pain medication since the last exercise session

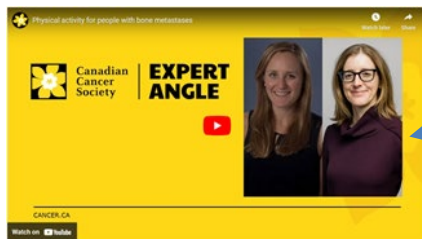
✓ = Target exercise region

^b exclusion of shoulder flexion/extension/abduction/adduction and inclusion of elbow flexion/extension

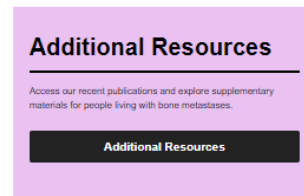
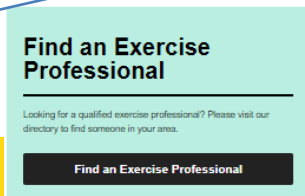
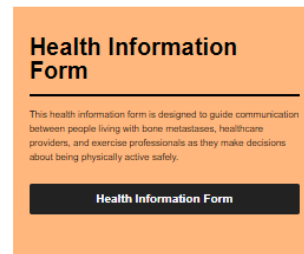
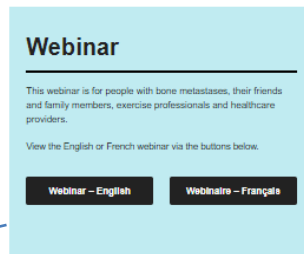
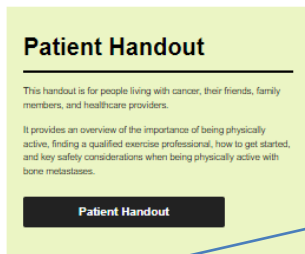
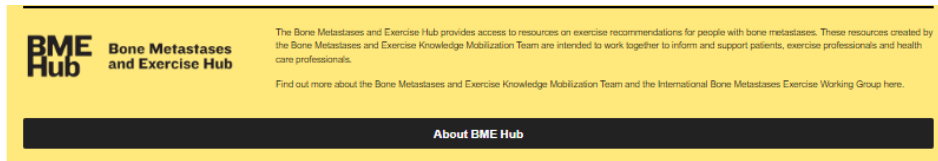
^c exclusion of hip extension/flexion and inclusion of knee extension/flexion

^d exclusion of spine/flexion/extension/rotation

WB weight bearing (e.g., walking), NWB non-weight bearing (e.g., cycling)



Wanting to do a **translation** or have a **link** in the BME website to own website → email Kristin Campbell.



Being physically active when you have bone metastases
An information form to help you for active safety.

The information summarized on this form can help you, your qualified exercise professional, and your healthcare team make decisions that are right for you about how to be physically active safely.

Physical activity for people with bone metastases can be:

- Safe when appropriately monitored by a qualified exercise professional.
- Beneficial and can improve fatigue, clinical function, and quality of life.

To be completed by patient: I consent to the release of my medical information outlined below.

Name (printed) _____ Date (month/year) _____

Signature _____

To be completed by healthcare team: This form will complement the health history and exercise screening questions asked by a qualified exercise professional.

Date (month/year) _____

Case of imaging attached: ☐ Yes ☐ No

Bone metastases location	Area of clinical concern	Current or planned treatment
<input type="checkbox"/> Cervical <input type="checkbox"/> Thoracic <input type="checkbox"/> Lumbar <input type="checkbox"/> Sacral <input type="checkbox"/> Skull <input type="checkbox"/> Ribs <input type="checkbox"/> Pelvis <input type="checkbox"/> Other (specify) _____	<input type="checkbox"/> Pain <input type="checkbox"/> Fracture <input type="checkbox"/> Spinal cord compression <input type="checkbox"/> Other (specify) _____	<input type="checkbox"/> Systemic therapy <input type="checkbox"/> Radiation therapy <input type="checkbox"/> Surgery <input type="checkbox"/> Other (specify) _____

Other general considerations for exercise professional:

☐ None
☐ Other (specify) _____

Exercise history (pathological fractures):

☐ Yes
☐ No

Healthcare provider name: _____ Date (month/year): _____

If you experience any change in symptoms, such as pain, talk to your healthcare provider or qualified exercise professional.

The form information is provided as guidance for people with bone metastases and not intended to replace clinical judgment.



Currently available in 6 languages.

Methods

Primary endpoints:

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



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

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**

Trial successful if either or both are statistically significant.*

Baseline characteristics

Intervention group (n=178)



Age (years)
 54.9 ± 11.6



Female
99.4%



Endocrine treatment
>50%

Control group (n=179)



Age (years)
 55.9 ± 10.7



Female
99.4%



Endocrine treatment
>50%

Baseline characteristics

Intervention group (n=178)



Age (years)
54.9 ± 11.6



Recurrent disease
65.1%



Female
99.4%



1st/2nd line
75.3%



Endocrine treatment
>50%



Bone metastases
65.2%

Control group (n=179)



Age (years)
55.9 ± 10.7



Recurrent disease
62.1%



Female
99.4%



1st/2nd line
74.3%



Endocrine treatment
>50%



Bone metastases
69.8%

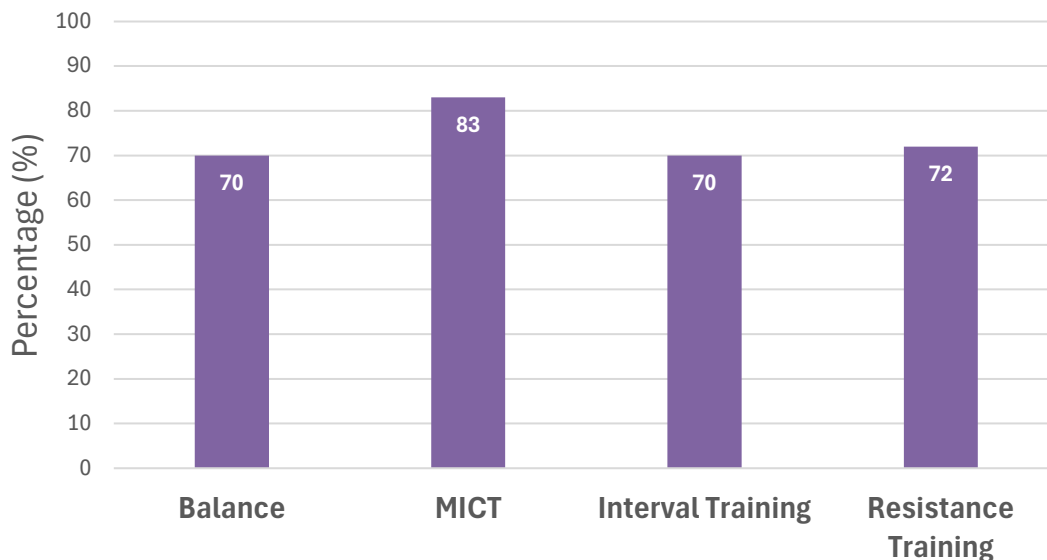
Results – Adherence and SAEs



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

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

Median Compliance



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

RESULTS

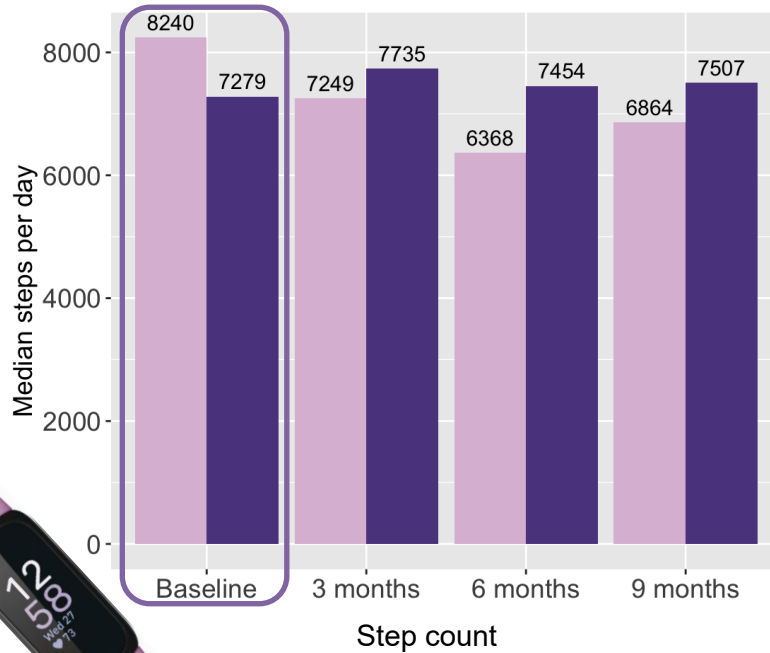
Physical activity & fitness



Results – Physical activity behavior

Control group
Exercise group

Measured physical activity (Fitbit)

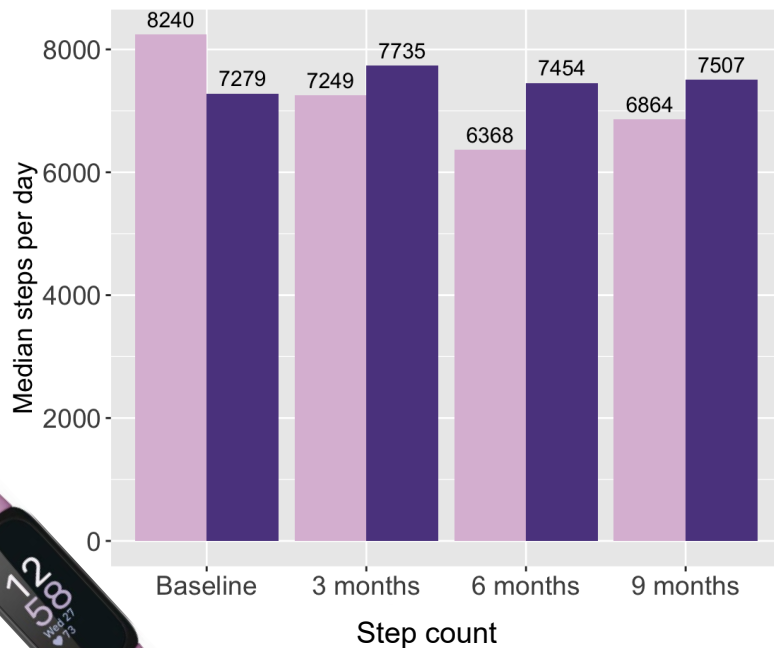


★ Significant between-group differences

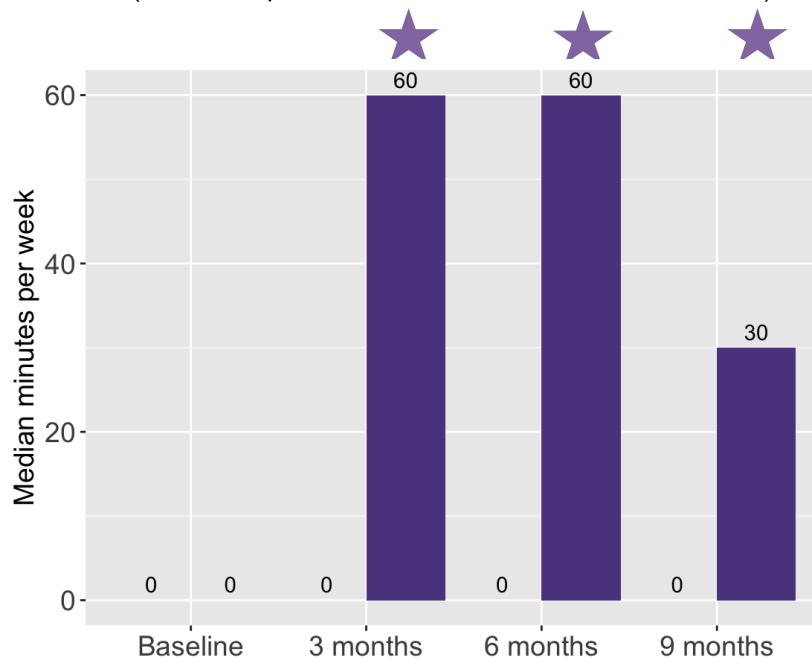
Results – Physical activity behavior

Control group
Exercise group

Measured physical activity (Fitbit)



Self-reported **resistance** exercise (Godin-Shepard Leisure-Time Exercise Questionnaire)

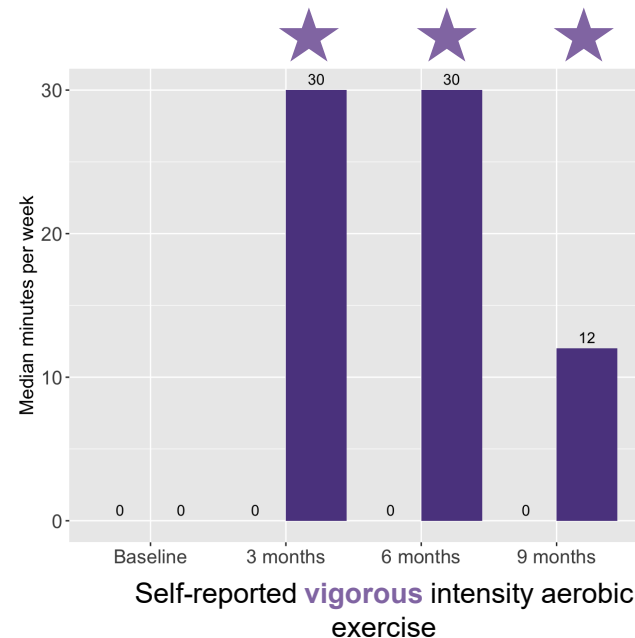
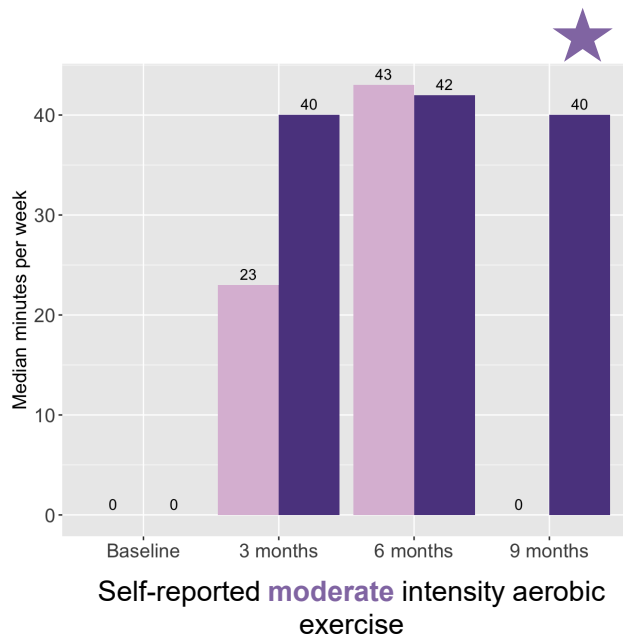


★ Significant between-group differences

Results – Physical activity behavior

Self-reported physical activity
(Godin-Shepard Leisure-Time Exercise Questionnaire)

Control group
Exercise group



Fitbit data confirm these findings.

★ Significant between-group differences

Results – physical fitness outcome

Physical fitness

Physical performance

Muscle strength

Aerobic capacity –
Endurance Test



Short-Fullerton Advanced
Balance Scale



h1-RM legpress



Maximal Short Exercise
Capacity – Steep Ramp Test



5-times Sit-to-Stand



Hand Grip Strength

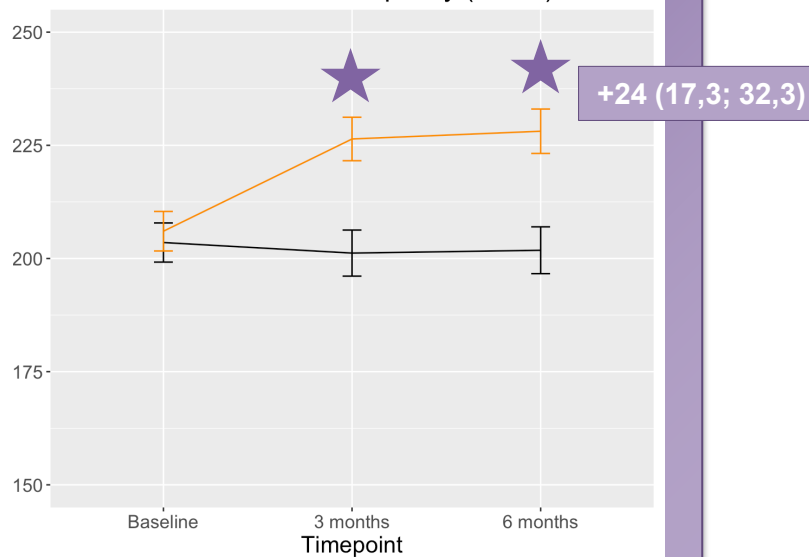


Results – Physical fitness

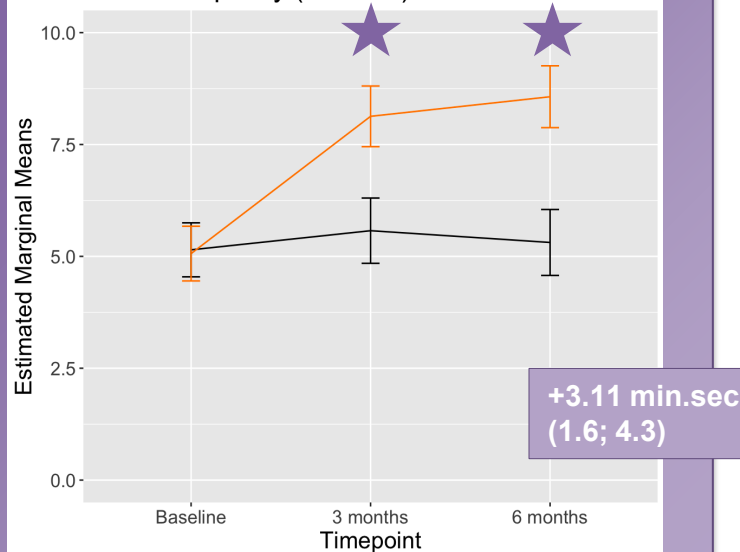


Control Group
Intervention Group

Maximal Short Exercise Capacity (Watts)

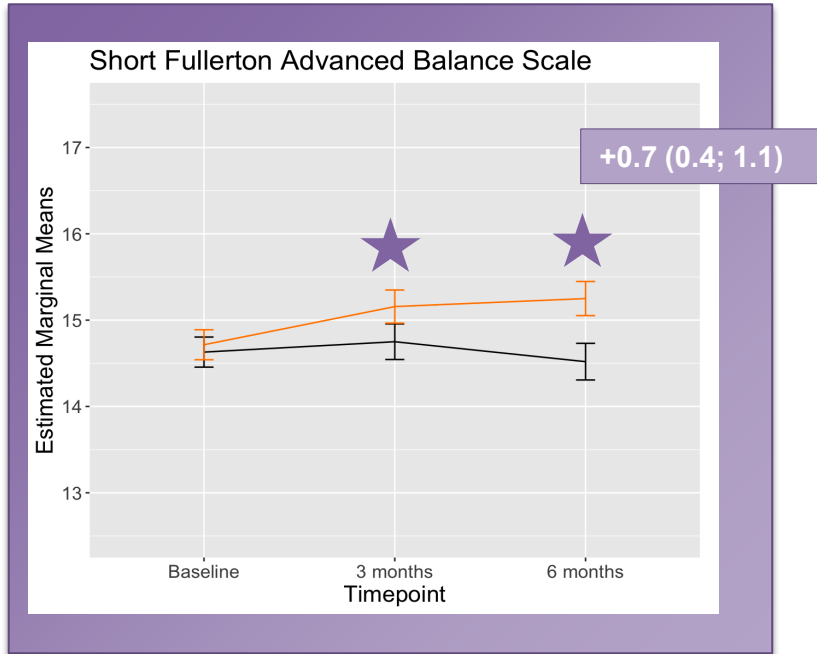


Aerobic capacity (minutes)

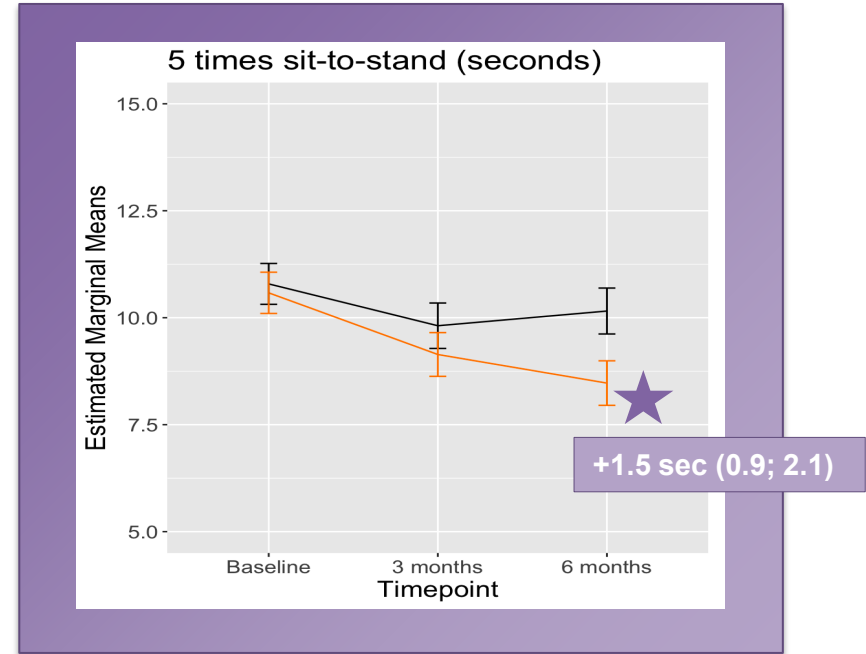


★ Significant between-group differences

Results – Functional performance

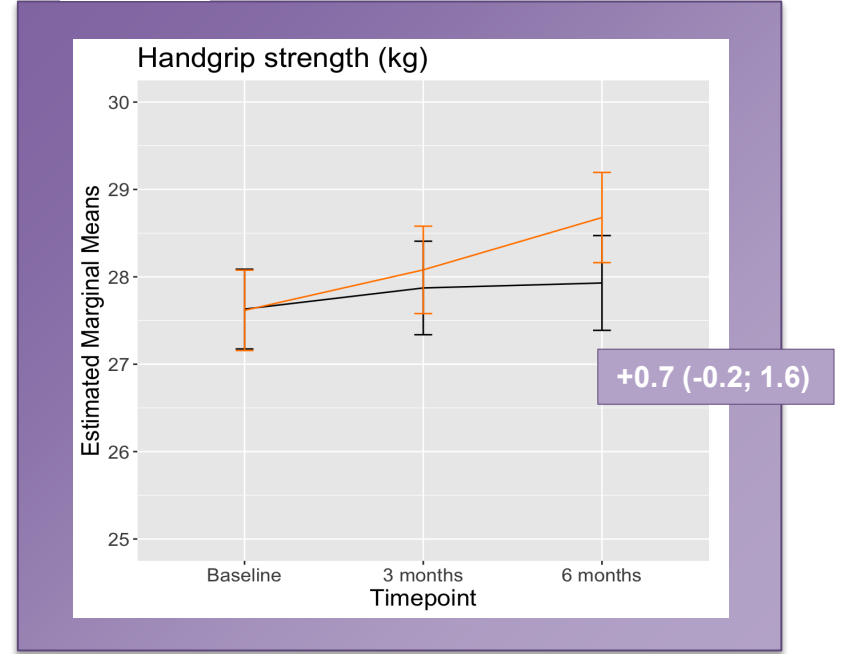
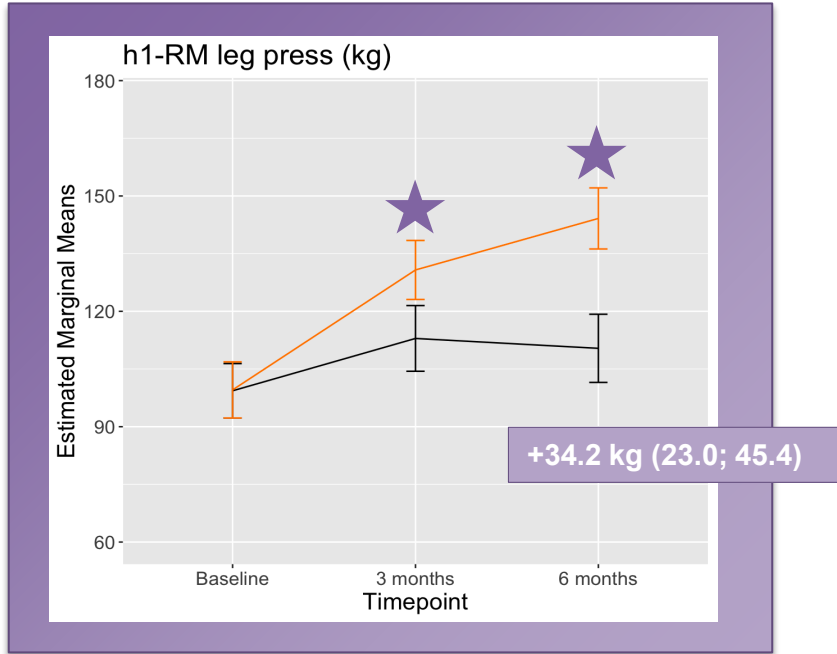


Control Group
Intervention Group



★ Significant between-group differences

Results – Muscle strength



Control Group
Intervention Group

★ Significant between-group differences

RESULTS

Patient-Reported Outcomes (PROMs)

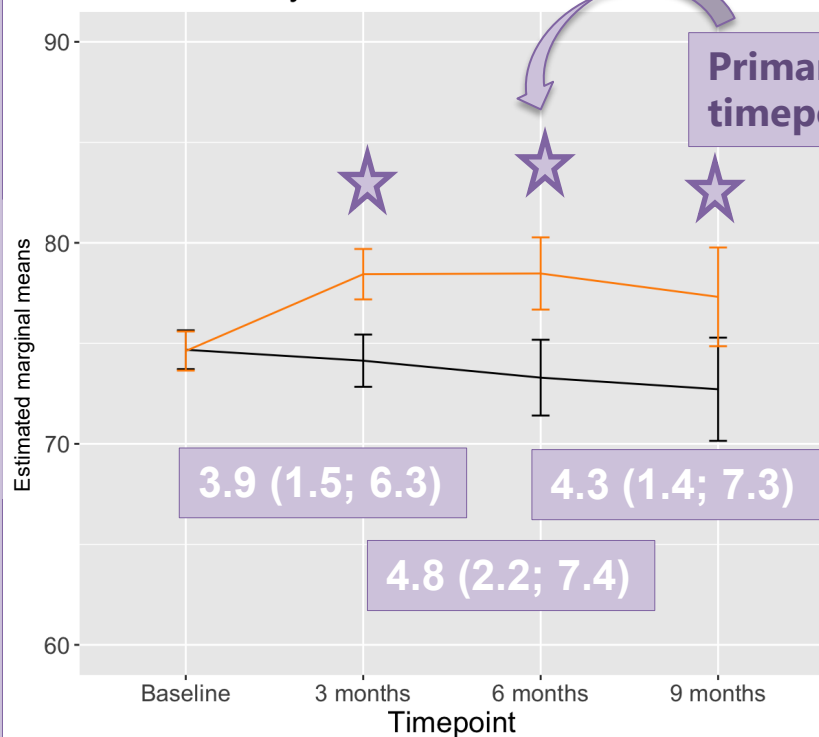


Primary outcomes

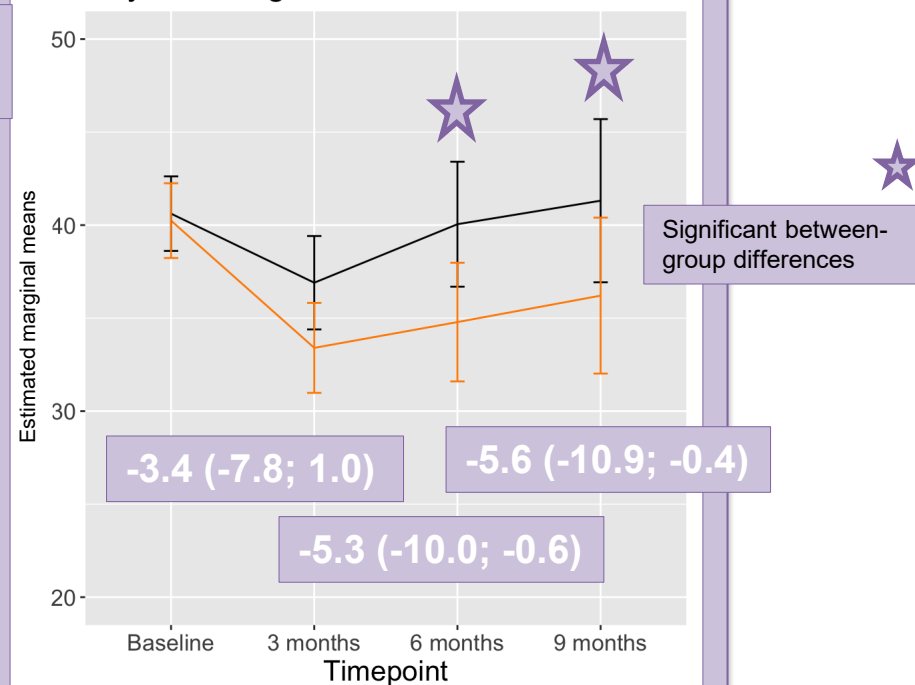
Randomization group

— Control Group
— Intervention Group

QoL Summary score



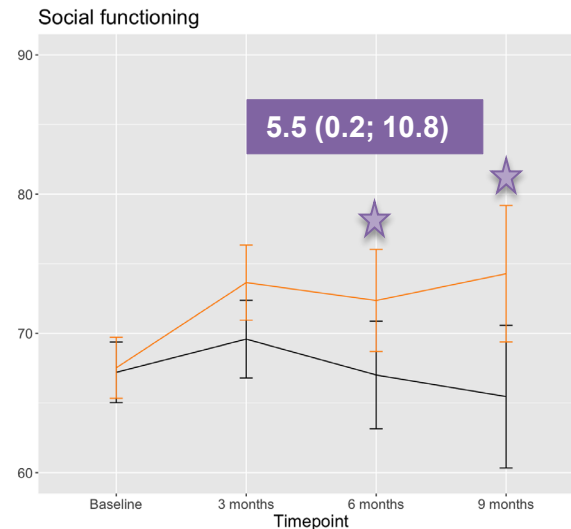
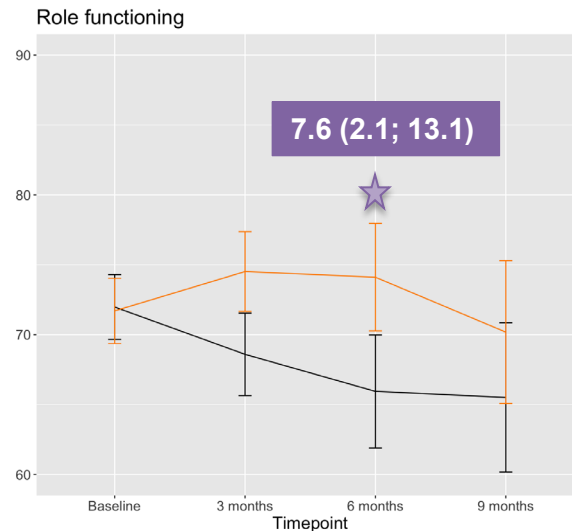
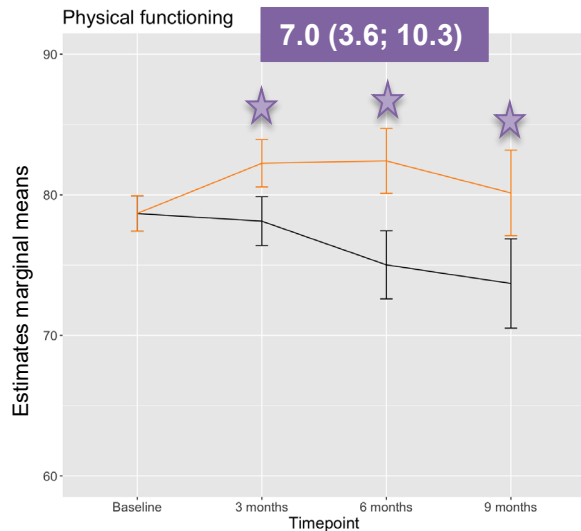
Physical fatigue



Results – QoL functional scales

Randomization group

— Control Group
— Intervention Group



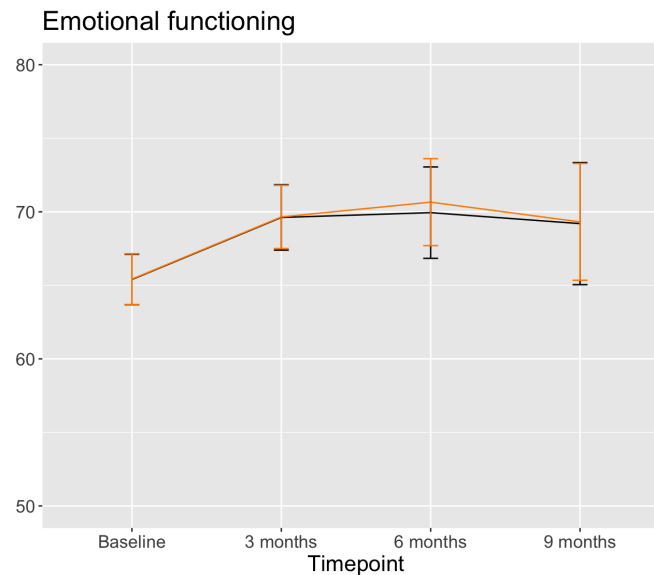
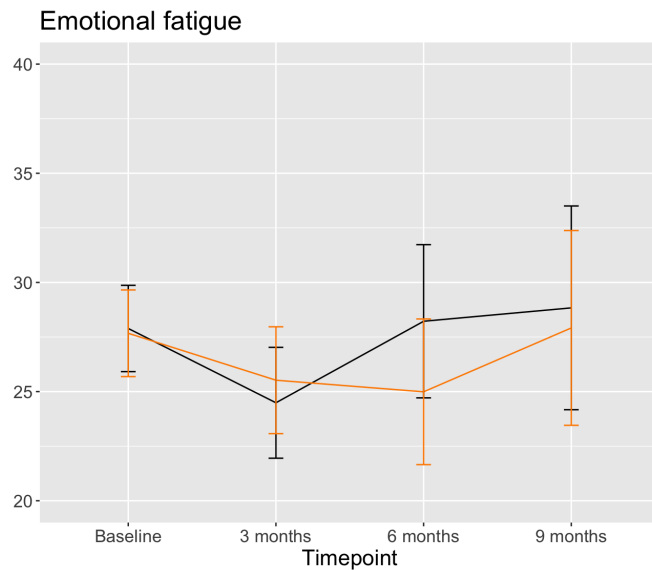
★ Significant between-group differences



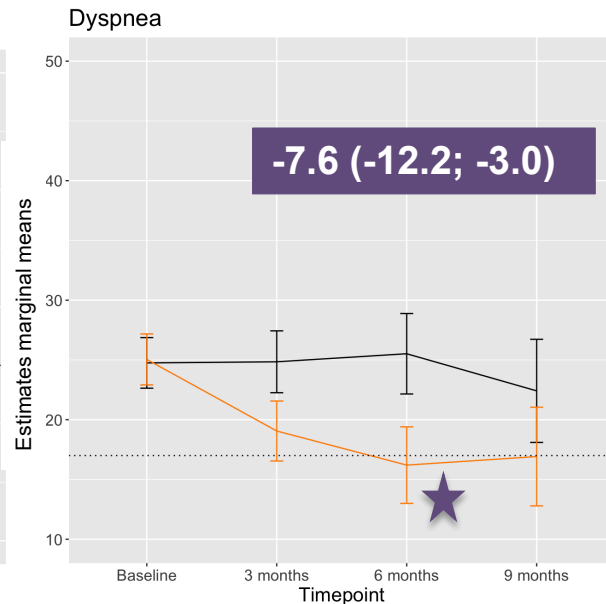
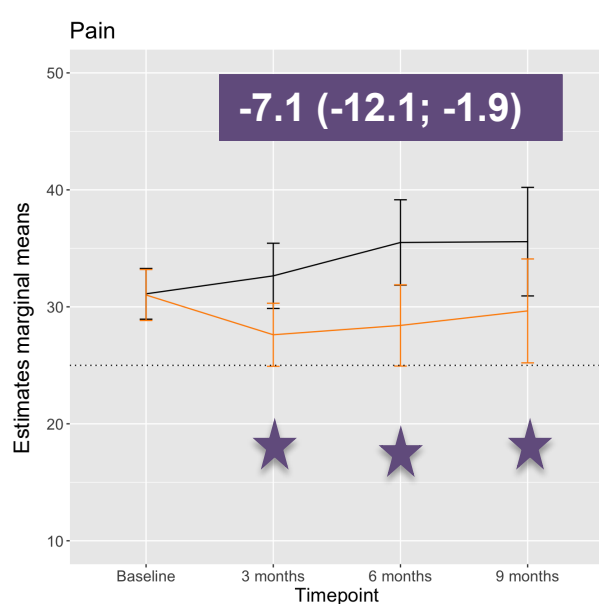
Results – Emotional fatigue and functioning

Randomization group

- Control Group
- Intervention Group



Pain and dyspnea



**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*

* Giesinger et al. J Clin Epidemiol. 2020

57%

Randomization group

— Control Group
— Intervention Group

Pain

Dyspnea

Conclusions

- A **supervised resistance and aerobic exercise** intervention resulted in beneficial effects on **fatigue, HRQoL, physical fitness, sexual health** and **other clinically relevant outcomes** of patients with mBC.



Conclusions



- Exercise for patients with mBC **decreases costs**.
- Both individual and group supervision are likely to be **cost-effective**.
 - **Group supervision** even more so.
- We believe that supervised exercise should be **reimbursed** for patients with mBC.

We recommend supervised exercise as part of supportive care regimens during mBC treatment

Stay tuned!
www.h2020preferable.eu

Publications



nature medicine



Article

<https://doi.org/10.1038/s41591-024-03143-y>

Supervised, structured and individualized exercise in metastatic breast cancer: a randomized controlled trial

Anouk E. Hiensch^{1,2,4}, Johanna Depenbusch^{2,3,4}, Martina E. Schmidt^{2,5}, Evelyn M. Monninkhof¹, Mirela Pelaez^{1,4}, Dorothea Clauss¹, Nadira Gunasekara^{2,6}, Philipp Zimmer¹, Jon Belloso², Mark Trevaskis¹, Helene Rundqvist^{2,7}, Joachim Wiskemann^{2,8}, Jana Müller^{2,9}, Maike G. Sweepers^{2,10}, Carlo Fremd^{2,11,12,13}, Renske Altena¹⁴, Maciej Gorecki¹⁵, Rhodé Bijlma¹⁶, Lobke van Leeuwen-Snoeks¹⁷, Daan ten Bokkel Huinink¹⁸, Gabe Sonke^{2,19}, Ainhara Lahuerta², G. Bruce Mann²⁰, Prudence A. Francis^{2,21}, Gary Richardson², Wolfram Malter²², Elsen van der Wal²³, Neil K. Aaronson²⁴, Elzbieta Senkus^{2,25}, Ander Urruticoechea², Eva M. Zopf^{2,26}, Wilhelm Bloch², Martijn M. Stuiver²⁰, Yvonne Wengstrom²⁷, Karen Steindorf^{2,28} & Anne M. May^{2,29}



Cost-effectiveness results are accepted in
Journal of Clinical Oncology.





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