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Physical exercise interventions in cancer survivors

Effects and methodological issues

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I have no disclosures.



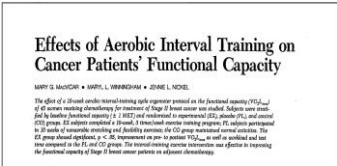
Advice to rest and avoid exercise



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Late 1980s
First (small) exercise study (n=24)



Beneficial effects on fitness, body composition, nausea



1990s
Few studies, clinical practice unchanged



2000 onwards:
Increase in # of studies and attention in clinical practice

2003: cancer exercise recommendations (American Cancer Society)



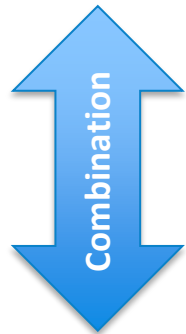
Content exercise interventions:

- Diverse and no consensus about optimal intervention

- **Types of interventions:**

- **Supervised interventions (2-3/week):**

- Aerobic exercise
(30-45 mins/session, moderate-to-high intensity)
- Resistance exercise
(about 10 exercises, 60-70% of 1RM)
- Combined aerobic and resistance exercise



- **Home-based interventions:**

- Walking
(e.g. 5 d/week for 20-30 mins, low-to-moderate intensity)
- Resistance exercises
(body weight or elastic bands)



Effects of exercise after cancer diagnosis

- Aim:
 - During treatment: Prevention of side effects (e.g., fatigue, ↓ fitness)
 - After treatment: Improvement of fitness, fatigue, QoL
 - Mechanistic studies: e.g., effects on bloodmarkers (immune system, etc)
- Beneficial effects on disease and treatment related side effects
 - Cardiorespiratory fitness and muscle strength ↑
 - Fatigue, sleep disturbances and depression ↓
 - Quality of life ↑
 - Body composition ↑
 - Inflammation ↓
 - Chemotherapy completion rate ↑

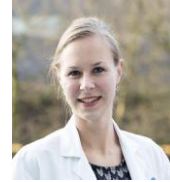
(Courneya et al. (2007); van Waart et al. (2015))



- Although conclusion of meta-analyses are positive, future research needed for:

- Patients with rarer type of cancer

e.g. ongoing PERFECT study (oesophageal cancer, abstract # 17)



- Patients with advanced disease

- Specific side effects (cognitive complaints (PAM study), osteoporosis, side-effects from novel targeted therapies)



- Focus on cancer outcomes (progression and survival)

e.g. ongoing CHALLENGE RCT (colon cancer, Arneya et al. CEBP 2016)

- Focus on optimal dose, intensity, type, timing of exercise

BUT:
One size does not fit all

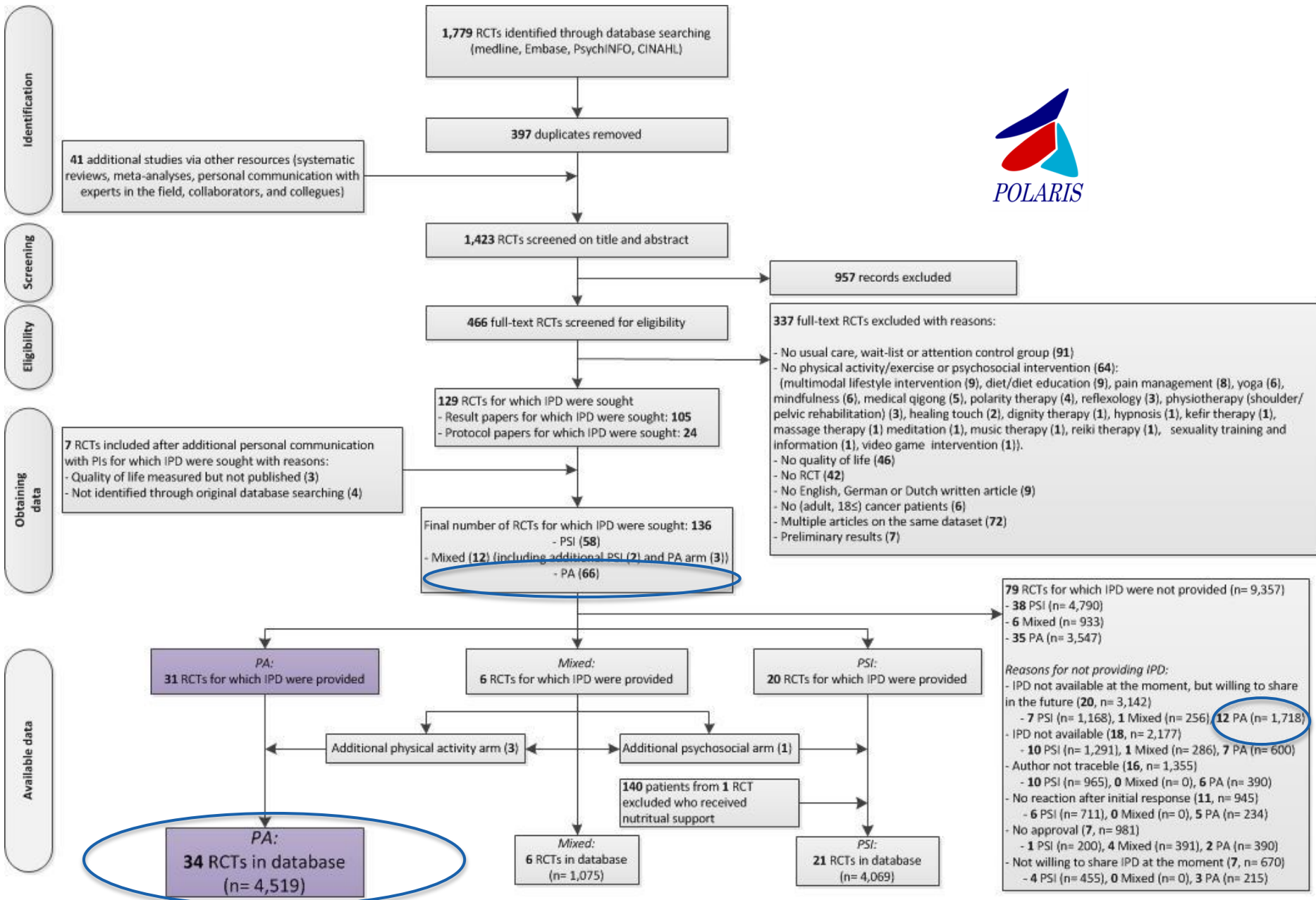


Predicting Optimal cAncer Rehabilitation and Supportive care

- Internationally shared database for individual patient data (IPD) meta-analyses
- Aim:
 - evaluate the effect of exercise interventions on quality of life
 - identify important demographic, clinical, personal, or intervention-related moderators of the effect;
 - build and validate clinical prediction models identifying the most relevant predictors of intervention success.

→ Personalised programs





Characteristics

	Intervention (n= 2,514)	Control (n=2,005)
Age, mean (SD) years	54.6 (11.5)	54.5 (11.2)
Women, n (%)	1961 (78.0)	1567 (78.2)
Cancer Type, n (%)		
Breast	1757 (69.9)	1406 (70.1)
Male genitourinary	326 (13.0)	248 (12.4)
Haematological	199 (7.9)	195 (9.7)
Gastrointestinal	146 (5.8)	87 (4.3)
Gynaecological	44 (1.8)	33 (1.6)
Respiratory track	28 (1.1)	29 (1.4)
Other	14 (0.6)	7 (0.3)
Timing of intervention, n (%)		
Pre-during-post treatment	80 (1.8)	
During treatment	2122 (47.0)	
Post-treatment	2314 (51.2)	

Effects on QoL using individual patient data

- Positive effects on QoL and physical functioning
- No demographic & clinical & intervention –related moderators were found
→ PA is equally effective across subgroups
- Effect of supervised exercise intervention larger when compared to unsupervised exercise (p for interaction $< 0,05$)

Next steps:

- Cancer specific analyses
- (Moderating) effects on fatigue, physical fitness, other psychosocial and clinical outcomes

PART 2: Methodological challenges in exercise oncology research:

Blinding not possible:

- Difficult accrual
- Drop-out after randomization to control
- Contamination between study arms (mainly non-compliance in the control group)





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UMBRELLA Fit study

cohort randomized controlled trial (cmRCT) on effects of exercise on quality of life of patients with breast cancer

Anne May, Roxanne Gal, Evelyn Monninkhof, Petra Peeters, Carla van Gils, Lenny Verkooijen, Desirée van den Bongard, Marco van Vulpen

Informed consent UMBRELLA cohort

1. Collection of clinical data and patient reported outcomes

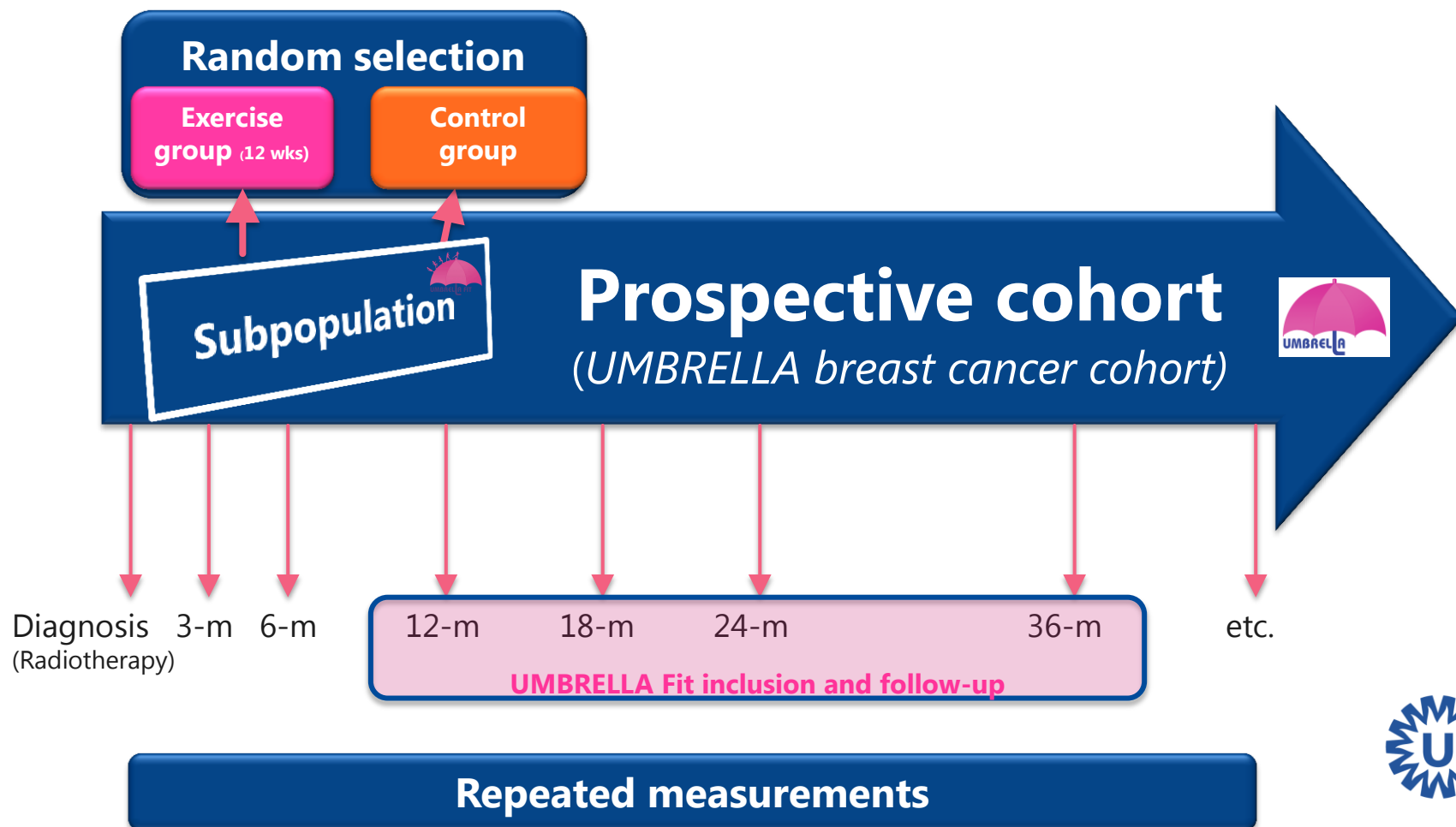
Optional:

2. Randomization to future interventions

UMBRELLA Fit trial

cmRCT design

(Relton et al. BMJ 2010)



cmRCT design

Possible benefits

- ✚ Control group unaware of the trial
 - ↳ Less drop-out after randomisation
 - ↳ Less contamination (non-compliance)
 - ↳ Better reflection of the real world (pragmatic)
- ✚ Study within UMBRELLA cohort
 - ↳ Faster recruitment
 - ↳ Long-term effects
- ✚ Less selective population

Possible disadvantages

- ✚ Higher drop-out rate intervention group
 - ↳ Non-compliance (decline intervention)
 - ↳ Drop-out during intervention
- ✚ Restricted to data from cohort
 - ↳ Definition of subpopulation
 - ↳ Outcome measurements

Present state of research (Aug 2016)



Randomized ($N = 166$)

Age: 58.0 ± 9.2 | PA*

Intervention ($N = 53$)

Control group ($N = 53$)

Age: 57.6 ± 9.6

($N = 30$; 57%)

Age: 58.0 ± 9.3

"Maybe later"
($N = 6$; 11%)

Age: 60.7 ± 7.7

"No"
($N = 17$; 32%)

Age: 58.5 ± 8.3

Results expected in 2017



* Physical activity = cycle to work and during leisure time (moderate/fast), walking during leisure time (fast) & sports (> MET 4.0)

Conclusion

- Overall exercise interventions are beneficial
- Research should focus on targeted interventions, intervention characteristics, special side-effects, specific types of cancer, mechanisms, cancer prognosis
- If feasible, cmRCT design might facilitate exercise research



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