Physical training as a way to reduce the burden from late effects, - a review of the literature.

Aarhus Breast Surgery Workshop 2022

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About breast cancer

- The most prevalent cancer among women
- Each year about 4500 women are diagnosed with breast cancer in DK
- The survival rate have been increasing over the last decades
- Today more then 70.000 women are living after a breast cancer diagnosis in DK



Improved and increased treatment

• Surgery,	100%
 Radiotherapy, 	80%
 Chemotherapy, 	40%
 Endocrine therapy, 	80%
 Antibody treatment, 	20%
 Immune therapy, 	-
• Bisphosphonate treatment,	60%





Late effects after a breast cancer diagnose

General late effects after cancer and cancer treatment

Specific locoregional late effects Late effects after the specific systemic treatment

Treatment induces secondary diseases



Δ

Physical activity as an intervention

- Studies in healthy (and elderly) populations have shown:
 - Improved cognitive function
 - Decrease the risk of developing osteoporosis
 - Seem so slow down the progression of dementia
 - A cornerstone in cardiac rehabilitation





What is physical activity ?

- Resistance training
- Aerobic training
- Specific training elements
- Rigorous activity



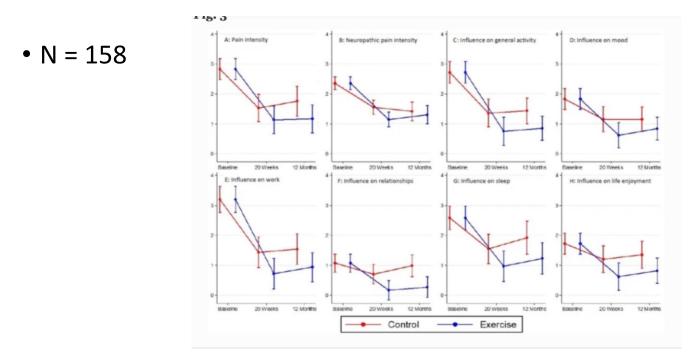
Relevant late effects for physical interventions

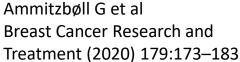
- Arm and shoulder morbidity
- Lymph eodema
- Fatigue
- Cognitive impairment
- Poly-neuropathy



Persistent pain and physical activity

• A randomised study of the effect of resistence training on "post surgery" pain







Physical training and menopausal symptoms

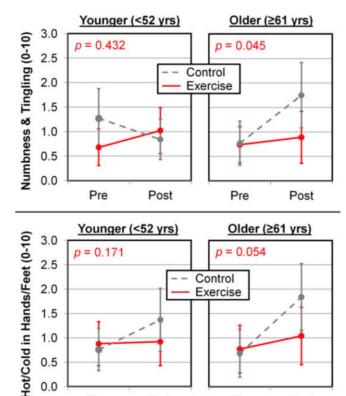
- Randomised study of a combined intervention:
 - Cognitive behavioural therapy (CBT) and physical exercise
- N = 422
- Results:
 - Positive effects on the perceived burden of hot flashes and night sweats (as assessed by the Hot Flush Rating Scale)
 - and on the level of sexual activity (a positive effect) were observed only in the groups that underwent CBT.



Duijts SFA et al *J Clin Onco, 2012 30:4124-4133.*

Physical activity and poly-neuropathy

- A randomised study of 355 cancer patients (79% breast cancer ptt)
- Intervention: a 6 weeks home based exercise program (walking and resistance exercise)



Post

Klaerkner IR et al Support Care Cancer. 2018 April; 26(4): 1019–1028



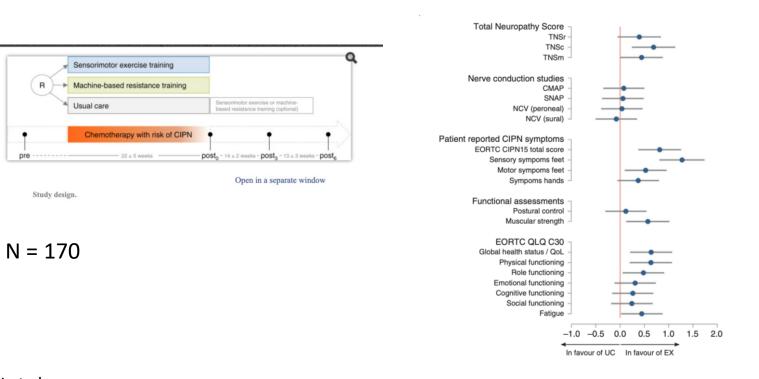
Post

Pre

0.0

Pre

Physical activity and poly-neuropathy





Müller J et al British Journal of Cancer (2021) 125:955–965

Physical activity and poly-neuropathy - a focused intervention

- A randomized study evaluating a specific intervention aiming at strengthen balance and postural stability.
- N= 36 breast cancer patients treated with paclitaxel
- Results showed a significant improvement in postural stability, but no impact upon general well-being or Quality of life

Vollmers PL et al Journal of Cancer Research and Clinical Oncology (2018) 144:1785–92



Physical training and fatigue

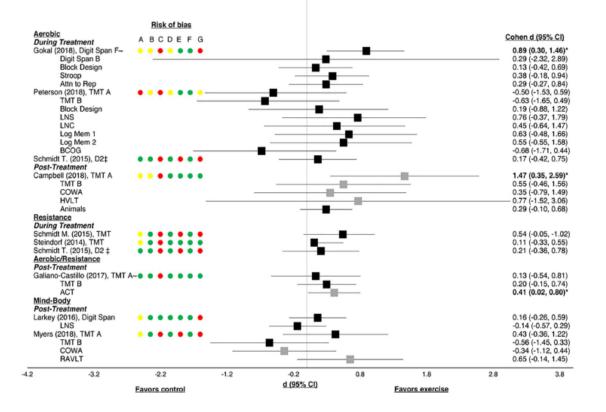
- 20 studies included, with a total of 1783 women
- Different interventions
- Results:
 - supervised resistance training and supervised intervention of combined resistance and aerobic training are the most effective in reducing fatigue, especially for women undergoing chemotherapy

Medeiros Torres D et al Supportive Care in Cancer (2022) 30:4651–4662



Physical training and cognitive problems

- a meta analysis of 29 trials



Cambell KL et al: Phys Ther 2020 Mar 10;100(3):523-542. The authors conclusion:

"More high-quality and appropriately powered randomized controlled trials designed to specifically evaluate the effect of exercise on cognitive function as the primary outcome, especially using objective outcome measures, are needed."



Motivation for engaging in physical activity - a meta analysis

			eriment			ontrol			Std. Mean Difference	Std. Mean Difference
-	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
ł	Post-intervention									
	Baruth 2015	42	9.167	18	37.9	9.167	12	4.2%	0.44 [-0.30, 1.18]	
	Pinto 2013a	42.2	5.81	19	41.9	5.57	24	6.3%	0.05 [-0.55, 0.65]	
	Pinto 2013b	43.29	7.94	89	42.17	8.02	84	24.1%	0.14 [-0.16, 0.44]	
	Vallance 2007	43.1	8.9	84	42.6	8.7	85	23.7%	0.06 [-0.25, 0.36]	
	Zhou 2017	40.7	8.77	61	37	8.26	52	15.8%	0.43 [0.06, 0.80]	
	Bennett 2007	19	2.9	20	18.54	3.64	26	6.7%	0.14 [-0.45, 0.72]	
	Nyrop 2017	5.17	2.87	24	5.23	2.82	29	7.8%	-0.02 [-0.56, 0.52]	
	Pinto 2005	72.92	21.41	39	57.72	26.2	43	11.4%	0.63 [0.18, 1.07]	
	Subtotal (95% CI)			354			355	100.0%	0.22 [0.06, 0.37]	◆
	Heterogeneity: Tau ² =	0.00; Cł	$hi^2 = 7.2$	9, df =	7 (P = 0	.40); l ² :	= 4%			
	Test for overall effect:	Z = 2.76	(P = 0.	006)						
	3 months follow-up									
3	Pinto 2013a	40.0	5.00	10	10.1			44.00/	0.501.000.4.041	
		43.3		19		5.55	23	14.0%	0.59 [-0.03, 1.21]	
	Pinto 2013b	42.6	7.9	86	40.71	8.08	80	58.0%	0.24 [-0.07, 0.54]	
	Pinto 2008 Subtotal (95% CI)	65.14	28.26	39 144	59.64	21.41	41 144	28.0% 100.0%	0.20 [-0.24, 0.64] 0.27 [0.04, 0.51]	
						50) 13		100.0%	0.27 [0.04, 0.51]	-
	Heterogeneity: Tau ² =				2(P = 0)	1.56); I ^z :	= 0%			
	Test for overall effect:	Z = 2.31	(P = 0.)	02)						
	6-9 months follow-up									
	Pinto 2013a	42.3	5	19	41.8	5.55	23	15.0%	0.09 [-0.52, 0.70]	
	Pinto 2013b	42.45	7.97	84	40.2	7.91	78	57.8%	0.28 [-0.03, 0.59]	
	Pinto 2008	67.25		39	54.68		39	27.2%	0.50 [0.05, 0.95]	
	Subtotal (95% CI)	07.20	20.40	142	01.00	2		100.0%	0.31 [0.08, 0.55]	•
	Heterogeneity: Tau ² =	0 00· Cł	$hi^2 = 1.2$		2 (P = 0	(55) [•] l ²				-
	Test for overall effect:				- (0		0 /0			
	root ion or of all offoot.	2.01	0.)						
										-2 -1 0 1 2
										Favours [control] Favours [experimental]

Supporting and counselling seem to be very important for the effect

FIGURE 2-Forest plot of the meta-analysis on fatigue after the intervention (A) at follow-up of 3 months (R) and at follow-up of 6 to 9 months (C) CI confidence interval.

		Experimental		c	Control			Std. Mean Difference	Std. Mean Difference		
		Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	IV, Random, 95% CI
	A	No/infrequent counseling									
		Vallance 2007	43.1	8.9	84	42.6	8.7	85	63.4%	0.06 [-0.25, 0.36]	-
		Bennett 2007	19	2.9	20	18.54	3.64	26	16.9%	0.14 [-0.45, 0.72]	
		Nyrop 2017	5.17	2.87	24	5.23	2.82	29		-0.02 [-0.56, 0.52]	
		Subtotal (95% CI)			128			140	100.0%	0.05 [-0.19, 0.29]	+
		Heterogeneity: Tau ² =				2(P = 0	.93); I ²	= 0%			
		Test for overall effect:	Z = 0.45	(P = 0.	66)						
HUIZINGA F et al. Med Sci Sports Exerc 2021 Dec 1;53(12):2661-2674	В	Frequent counseling Baruth 2015 Pinto 2013a Pinto 2013b Zhou 2017 Pinto 2005 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect:	42 42.2 43.29 40.7 72.92 0.01; Ch	7.94 8.77 21.41	61 39 226 1, df =	41.9 42.17 37 57.72		12 24 84 52 43 215 = 9%	10.7% 37.6% 25.6% 18.9%	0.44 [-0.30, 1.18] 0.05 [-0.55, 0.65] 0.14 [-0.16, 0.44] 0.43 [0.06, 0.80] 0.63 [0.18, 1.07] 0.32 [0.12, 0.52]	
		Test for subgroup diffe		01-12 - 0	. 70 . 44	- 1 (D	0.40	12 - 00			-2 -1 0 1 2 Favours [control] Favours [experimental]



Test for subgroup differences: Chi² = 2.70, df = 1 (P = 0.10), l² = 62.9%

FIGURE 3-Forest plot of the meta-analysis on fatigue for no or infrequent counseling (A) and frequent counseling (B). CI, confidence interval.

Different type of physical training

- In a meta analysis of 20 randomized clinical trials involving 1793 participants it was found that:
 - supervised combination of resistance training (RT) with aerobic training (AT) is the most effective physical exercise to reduce fatigue
 - the supervised RT was more effective than supervised AT or mind– body techniques.

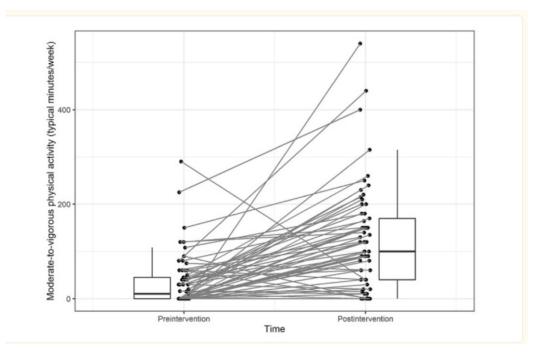
Medeiros Torres D et al. Supportive Care in Cancer (2022) 30:4651–4662



Can this be done via the Internet

• A study of 82 breast cancer survivors,

testing a internet based intervention based on the "Acceptance and Commitment Therapy" (ACT)



Robertson MC et al: JMIR Cancer. 2022 Apr-Jun; 8(2): e31815



Barriers for engaging in physical activity

- The participation rate in physical activity programs is often low
 - Lack of time
 - Lack of motivation
 - Lack of confidence (in how to perform training)
 - Feeling unwell or tired



Targeting activity or sedentary time

- In a study of 199 breast cancer survivors, where both amount of physical activity and sedentary time was assessed:
 - Moderate to vigorous physical activity let to decreased depressive symptoms
 - Sedentary time predicted level of pain and depressive symptoms
 - More sedentary time higher scores on pain and depression

Dore I et a.l Supportive Care in Cancer vol 30, 785–792 (2022)



Relevant end points

- Quality of life
- Patient reported outcome
 - Fatigue
 - Pain
 - Depressive symptoms
- Objective measurements
 - Muscle strength
 - Cardiorespiratory fitness
 - Sedentary time?



Challenges when drawing conclusions

- Small sample sizes
- Many different end-points
- Different measures
- Different intervention



Conclusion

- Physical activity is a promising intervention
- Physical activity seem to be able to alleviate late effects
 - It is cheap
 - It is with-out side effects
- Possibilities for (supervised) physical activity should be established
- More knowledge about what kind of physical activity is most effective



Thank you for Your attention

Questions !

