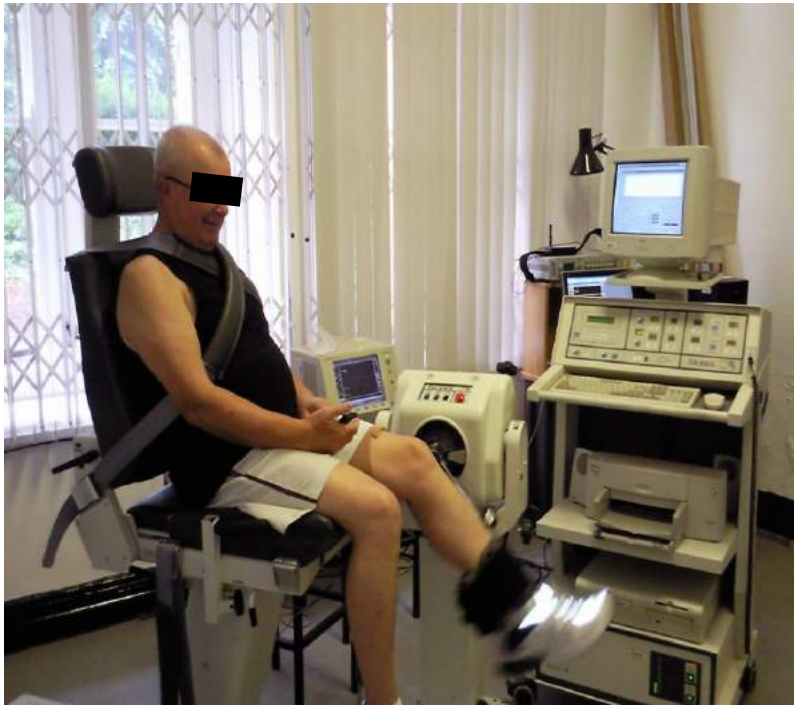
Pragmatic lifestyle interventions

What are the health benefits of pragmatically-implemented interventions (3-6 months) involving manageable amounts of supervised/home-based exercise and healthy eating advice in prostate and breast cancer patients?

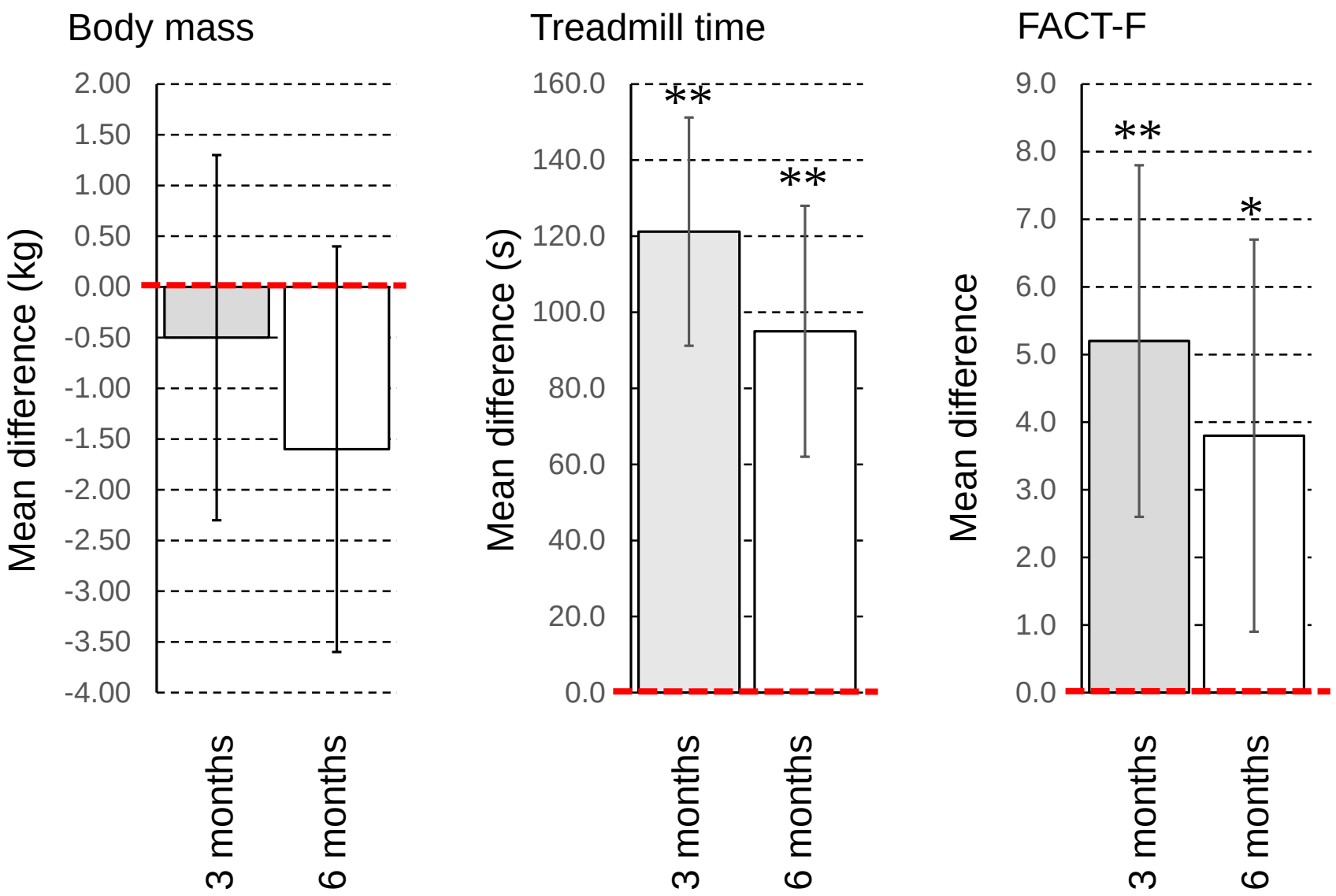
Exercise and dietary intervention in men with locally advanced & metastatic prostate cancer receiving androgen deprivation therapy

Internal pilot: Bourke L, Doll H, Crank H, Daley A, Rosario DJ, Saxton JM (2011). *Cancer Epidemiol Biomarkers Prev. 20, 647-57*.

RCT: Bourke L, Gilbert S, Hooper R, Steed LA, Joshi M, Catto JW, Saxton JM, Rosario DJ (2014). *Eur Urol 65, 865-72.*



- *Supervised and home-based aerobic and resistance exercise training 3-5 times per week for 12 weeks*
- *3 month unsupported phase*
- *Nutrition advice pack encouraging reduction of saturated fat and refined carbohydrate and increase of dietary fibre intake with moderation of alcohol*
- *Fortnightly, small-group healthy eating seminars*


Body mass
Mean difference (kg)
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
-3.00
-3.50
-4.00
3 months
6 months
Treadmill time
Mean difference (s)
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
**
**
3 months
6 months
FACT-F
Mean difference
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
**
*
3 months
6 months

Blood-borne biomarkers at baseline and after 3 months (internal pilot)

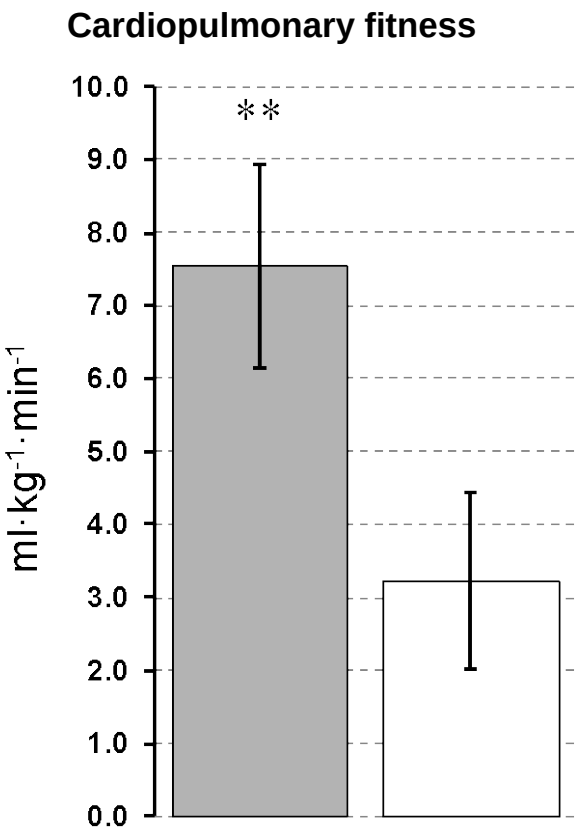
		Baseline		End-point			
	(n)	Usual care Mean (SD)	Intervention Mean (SD)	Usual care Mean (SD)	Intervention Mean (SD)	Group mean difference in Δ (95% CI)	*P*
Insulin ($mU.L^{-1}$)	42	10.8 (12.7)	10.4 (13.2)	11.7 (14.2)	8.91 (8.4)	-2.3 (-12.5, 7.8)	0.46
IGFBP3 ($ng.ml^{-1}$)	42	3052.5 (750.7)	3098.1 (738.2)	2964.7 (796.2)	2875.7 (827.3)	-134.6 (-503.9, 234.6)	0.49
IGF-1 ($ng.ml^{-1}$)	42	77.6 (25.8)	74.5 (21.5)	79.4 (27.2)	78.3 (22.6)	1.9 (-6.9, 10.8)	0.72
IGFBP-1 ($ng.ml^{-1}$)	42	34.5 (24.4)	32.6 (25.9)	38.4 (26.2)	36.4 (26.4)	-0.18 (-12.1, 11.7)	0.91
PSA ($ng.ml^{-1}$)	50	5.02 (10.2)	3.32 (6.83)	6.24 (13.6)	4.55 (8.74)	0.01 (-2.2, 2.2)	0.61
Serum Testosterone ($nmol.L^{-1}$)	40	3.19 (6.97)	4.12 (8.69)	3.85 (8.67)	4.50 (8.01)	-0.28 (-1.8, 1.2)	0.68
Free Androgen Index	39	8.52 (19.4)	12.4 (24.3)	9.44 (21.5)	13.5 (22.8)	0.22 (-3.3, 3.8)	0.87
SHBG ($nmol.L^{-1}$)	40	45.1 (13.6)	41.6 (13.2)	46.8 (14.0)	40.8 (11.8)	-2.5 (-6.4, 1.5)	0.13

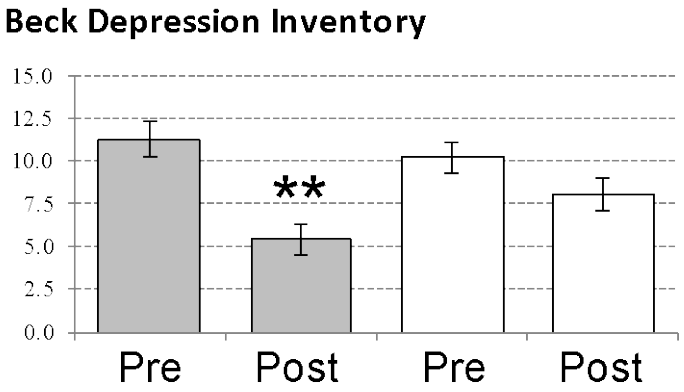
Exercise and hypocaloric healthy-eating intervention in overweight women recovering from early-stage breast cancer treatment

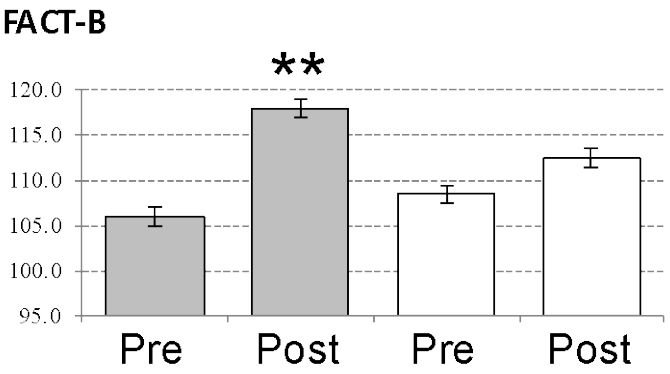
Scott E, Daley AJ, Doll H, Woodroofe N, Coleman RE, Mutrie N, Crank H, Powers HJ, Saxton JM (2013). *Cancer Causes Control 24, 181-191.*

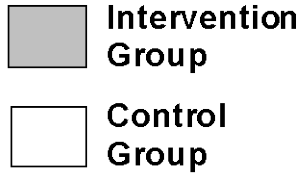
Saxton JM, Scott EJ, Daley AJ, Woodroofe M, Mutrie N, Crank H, Powers HJ, Coleman RE (2014). *Breast Cancer Res 16, R39.*

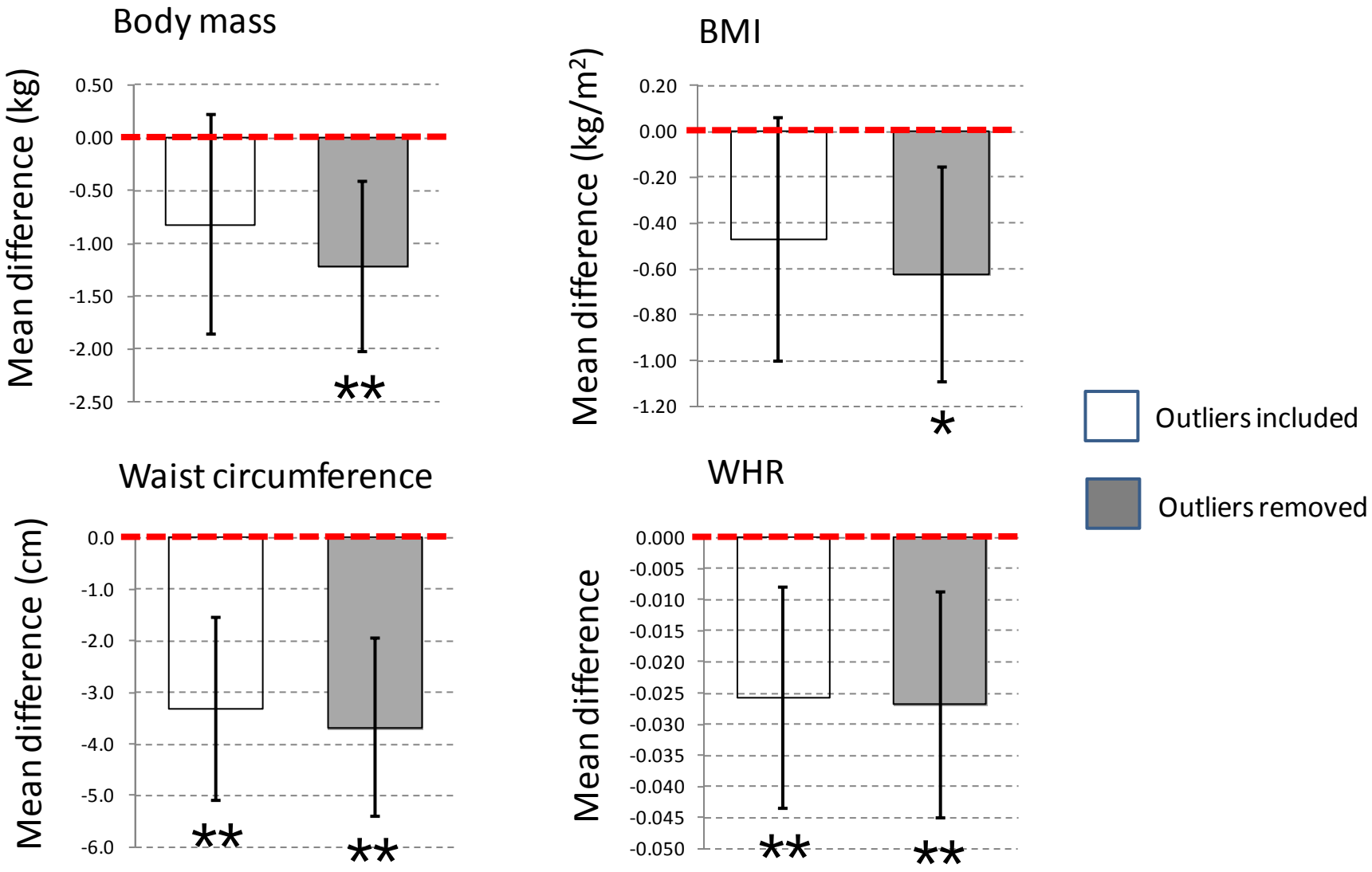
- *3 x weekly 30 min sessions of aerobic exercise using gym ergometers*
- *Resistance exercise (upper-body/trunk)*
  - *3 sets of 12 reps with light hand-held weights/resistance bands – arms, chest and back*
  - *Body weight resistance exercises, e.g. wall push-ups, etc.*
- *Encouragement to be more physically active/independent exercisers*
- *Personal nutrition advice based on achieving 600 kcal/day deficit and fortnightly group healthy eating sessions*


Cardiopulmonary fitness
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
**
ml·kg-1·min-1

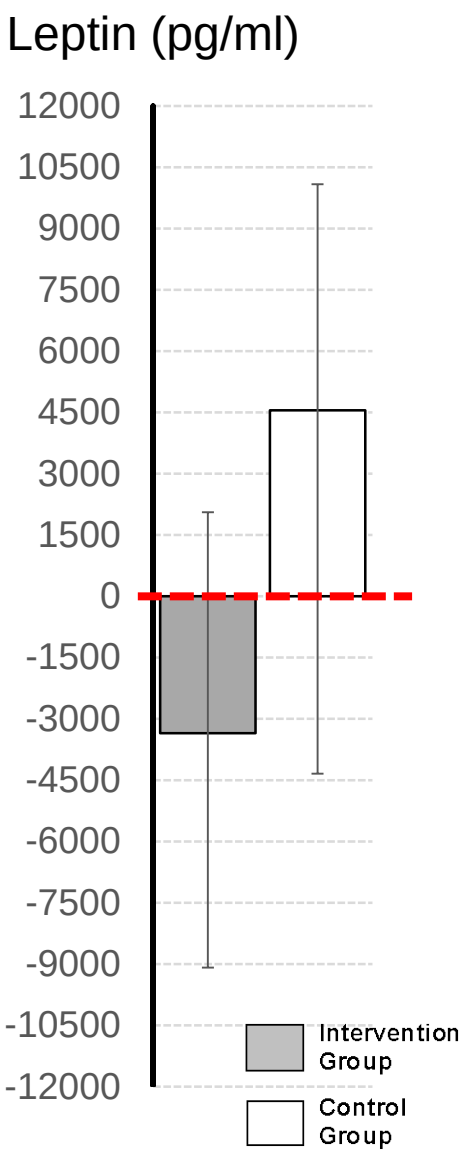

Beck Depression Inventory
15.0
12.5
10.0
7.5
5.0
2.5
0.0
**
Pre
Post
Pre
Post


FACT-B
120.0
115.0
110.0
105.0
100.0
95.0
**
Pre
Post
Pre
Post


Intervention Group
Control Group


Body mass
Mean difference (kg)
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
**
BMI
Mean difference (kg/m²)
0.20
0.00
-0.20
-0.40
-0.60
-0.80
-1.00
-1.20
*
Waist circumference
Mean difference (cm)
0.0
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
**
**
WHR
Mean difference
0.000
-0.005
-0.010
-0.015
-0.020
-0.025
-0.030
-0.035
-0.040
-0.045
-0.050
**
**
Outliers included
Outliers removed

Minimal effect on immune system



	Intervention group		Control group		*P*-value
	Baseline	Follow up	Baseline	Follow up	
Leukocyte counts					
Total leukocyte count (10^3 cells/μl)	5.145 (1.417)	5.156 (1.337)	5.184 (1.237)	5.594 (1.370)	**0.04**
Neutrophil count (10^3 cells/μl)	3.014 (1.119)	2.958 (1.135)	3.131 (0.912)	3.377 (1.061)	0.05
Monoctye count (10^3 cells/μl)	0.400 (0.370, 0.430)	0.400 0.360, 0.440	0.400 (0.350, 0.450)	0.400 (0.350, 0.450)	0.63
Lymphocyte count (10^3 cells/μl)	1.507 (0.414)	1.523 (0.389)	1.446 (0.497)	1.612 (0.449)	**0.04**
$CD3^+CD4^+$T cells (10^3cells/μl)	0.748 (0.596, 0.900)	0.682 (0.605, 0.759)	0.659 (0.532, 0.786)	0.763 (0.648, 0.878)	**0.02**
$CD3^+CD8^+$ T cells (10^3cells/μl)	0.474 (0.365, 0.583)	0.402 (0.334, 0.470)	0.360 (0.214, 0.506)	0.409 (0.322, 0.496)	0.05
$CD4^+$:$CD8^+$ ratio	1.62 (1.36, 1.88)	1.69 (1.40, 1.98)	1.93 (1.51, 2.35)	1.91 (1.49, 2.33)	0.87
NK cells (10^3 cells/μl)	0.200 (0.175, 0.225)	0.206 (0.177, 0.235)	0.176 (0.147, 0.205)	0.174 (0.144, 0.292)	0.46
Inflammatory cytokines					
IL-6 (pg/mL)	1.599 (1.259, 1.906)	1.692 (1.377, 2.007)	1.755 (1.456, 2.054)	1.942 (1.602, 2.282)	0.93
TNF-α(pg/mL)	0.889 (0.779, 0.999)	0.916 (0.767, 1.065)	1.058 (0.895, 1.221)	0.992 (0.870, 1.114)	0.61

No effect of on sex steroid hormones, insulin sensitivity, insulin-like growth factors/ binding proteins or *hs*-CRP.

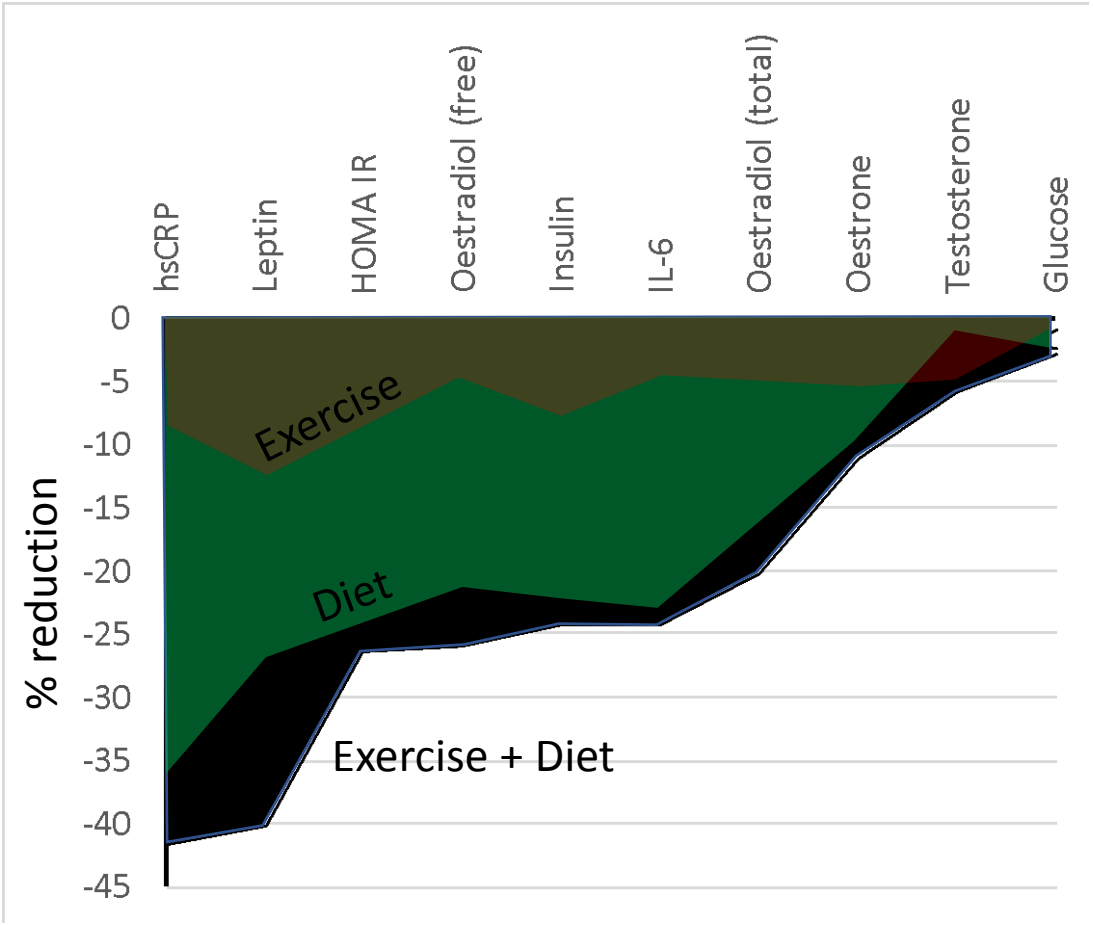
	Δ Body weight	Δ Waist circumference
Estradiol	−0.11	−0.14
Estrone	0.07	−0.13
Testosterone	0.09	0.06
SHBG	**−0.29****	**−0.31****
HOMA	0.21	0.12
IGF-1	−0.08	**−0.39****
IGFBP-1	−0.06	−0.14
IGFBP-3	**0.27***	0.14
Leptin	**0.36****	**0.35****
hs-CRP	**0.33****	**0.31****
Total cholesterol	**0.23***	0.19
HDL cholesterol	0.06	−0.01

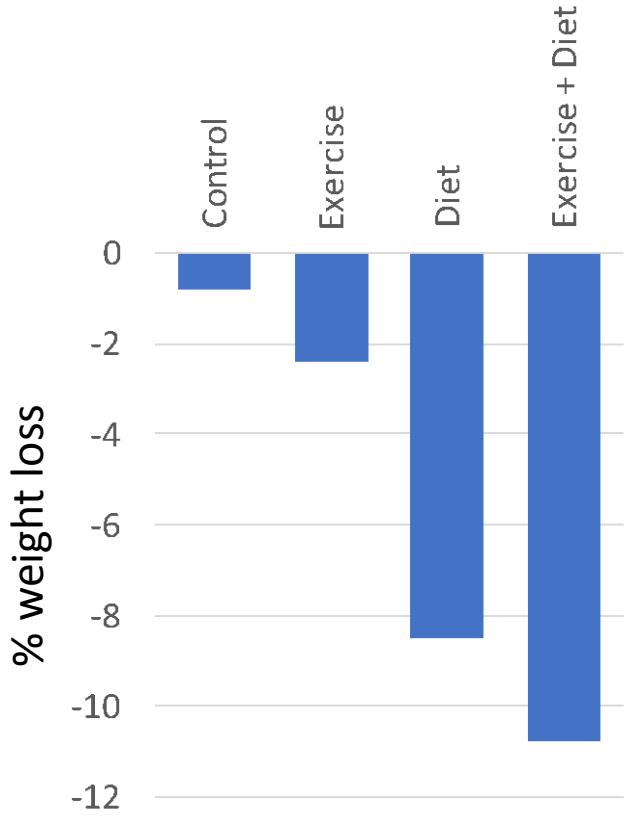
More intensive combined exercise and dietary interventions

Study details	*Weight loss*	*Changes in cancer-relevant biomarkers*
Pakiz *et al.* (2011); *Int J Behav Med 18, 333–341.* N=68 overweight/obese breast cancer survivors; 16 weeks of group-based D+E sessions versus control	6.8%	Non-significant reductions in IL-6 (p=0.06) and TNF-a (p=0.05).
Rock *et al*. (2013); *Clin Breast Cancer 13, 188–195.* N=258 overweight or obese breast cancer survivors; 18 months (first 6 months more intensive) group-based D+E sessions versus wait-list controls.	>5% versus <5%	Reductions in insulin, leptin, increased SHBG,
Travier *et al*. (2018); *Eur J Cancer Care, e12861.* N=42 overweight/obese breast cancer survivors; 12 weeks of group-based D+E sessions; single group pre- post-design.	7.7%	Reductions in glucose, insulin, C-peptide, HOMA-IR.
Imayama *et al*. (2012); *Cancer Res 72, 2314-2326.* N=439 overweight/obese post-menopausal women; 12 months of dietician-led group based D, E or D+E sessions versus control.	D+E: 10.8% D: 8.5% E: 2.4%	Reductions in hs-CRP, SAA and IL-6 in D & D+E groups with >5% weight loss; reduced leucocyte and neutrophil counts in D+E with >5% weight loss.
van Gemert *et al*. (2015). *Breast Cancer Res 17, 120.* N=243 overweight, inactive post-menopausal women; 16 weeks of dietician and physiotherapist group-based D (500 kcal/day deficit) or Mainly E (with 250 kcal/day deficit) sessions versus controls.	Mainly E: 6.9% D: 6.1%	Reductions in oestradiol, free oestradiol and SHBG in D and D+E groups; reduction in free testosterone in mainly E group; intervention effects were attenuated or disappeared after adjustment for changes in body fat.

McTiernan *et al*. 2011 – 2012

Multiple publications from the same study overweight/obese postmenopausal women: MVPA 45 min on 5 days per week and/or Hypocaloric diet





NEW-DAY
After Breast Cancer

Northumbria University NEWCASTLE

Sheffield Hallam University

yorkshire cancer research

North of England Women's Diet and ActivitY - After Breast Cancer Trial

(Acronym: NEW DAY-ABC)

NHS
The Newcastle upon Tyne Hospitals
NHS Foundation Trust

NHS
Gateshead Health
NHS Foundation Trust

NHS
Sheffield Teaching Hospitals
NHS Foundation Trust

Summary

- *Structured exercise and/or physical activity brings health benefits to cancer survivors that go beyond weight loss.*
- *Studies show that exercise can enhance the effects of dietary interventions on body composition and cancer-relevant blood-borne biomarkers in cancer survivors.*
- *The provision of comprehensive dietary support is also needed for clinically-important body fat reduction in overweight/obese cancer survivors.*

“Eating alone will not keep a man well; he must also take exercise… And it is necessary, as it appears, to discern the power of the various exercises, both natural exercises and artificial, to know which of them tends to increase flesh and which to lessen it…”

Hippocrates of Kos (c.460 – c.370 BC)
Regimen I