

Physical activity and cancer



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- Cancer prevention
- Less toxicity
- Less acute side effects
- Lower relapse
- Lower later degenerative disease





The NEW ENGLAND
JOURNAL of MEDICINE

Physical Activity and the Risk of Breast Cancer

Inger Thune, M.D., Tormod Brenn, M.Sc., Eiliv Lund, M.D., Ph.D., and Maria Gaard, M.D.

Prospective cohort study 25,000 women, 13.5 yrs

- 4 hours a week
- 30% reduction in breast cancer risk

N Engl J Med 1997; 336:1269



Exercise & Bowel cancer relapse

Australian cohort study, 526 patients, colorectal cancer 1990-4, recreational sport 1-2 week sweat and breathless. At 5 yrs

- 57% alive (non-exercisers)
- 71% alive (exercisers)
- statistically significant 14% ($p < 0.05$)

Giles GG, IARC Sci Publ, 2002. **156**: 69-70.



The National Cancer Institute

Meta-analysis of 45 observational studies:

- 2-3 hours of moderate PA / week is linked to a >30% reduction in relapse
- No study showed worse outcomes

Ballard-Barbash et al Nat Can Inst 2012



Davis & Thomas R BJC (2011) 105;52-9



Thomas & Holmes. BJMC (2014) 7: 1; 2-9.





Exercise-induced biochemical changes and their potential influence on cancer: a scientific review

Robert James Thomas, Stacey A Kenfield and Alfonso Jimenez

Br J Sports Med published online December 19, 2016



Direct biochemical pathway:

Indirect benefits



Weight reduction

Enhance Recovery Good Health for You (ENERGY)

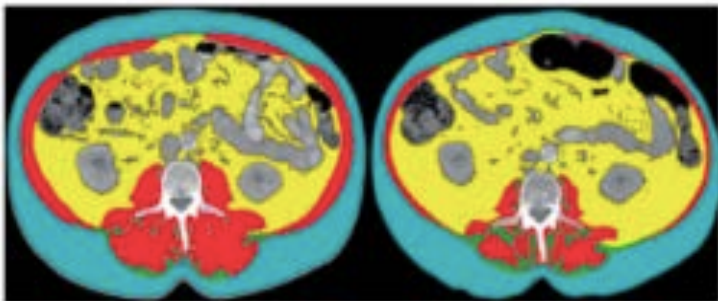
- Supervised exercise and dietary intervention programme
- Significant weight reduction at one year

Rock CL et al, JCO 2015

Sarcopenic obesity

ANNALS OF ONCOLOGY

- Low skeletal muscle mass,
- Low grip strength
- Slow gait speed.

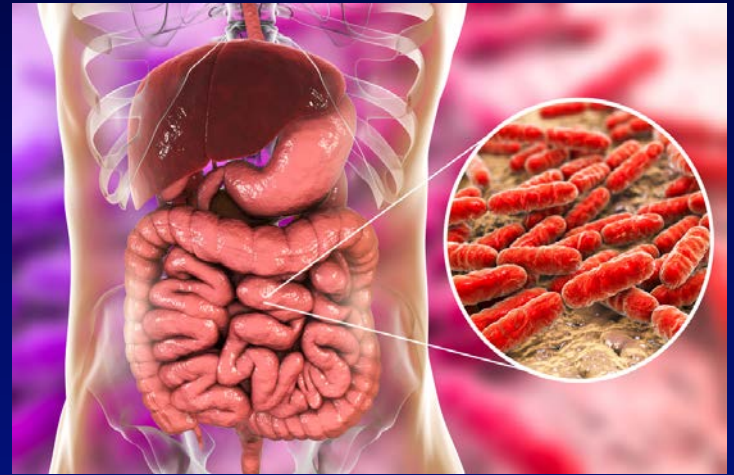


Cruz-Jentoft. Euro consensus on definition of Sarcopenia: Age Ageing. 2010;39(4):412.

Monoclonal antibodies (Ipilimumab, nivolumab)

- Better response rates
 - Better gut flora
 - Metastatic melanoma

THE UNIVERSITY OF TEXAS
MD Anderson
~~Cancer~~ Center



Reduce chronic inflammation

- Prostaglandins (PGE₂) made from arachidonic acid via COX-2
- COX-2 is induced by cytokines, tumour promoters
- Cancer progression, apoptosis, invasion, angiogenesis and metastasis
- Study involving rectal biopsies - increase in PA from 5.2 to 27.7 MET-hrs /wk 28% < mucosal PGE₂

Martinez et al 1999.

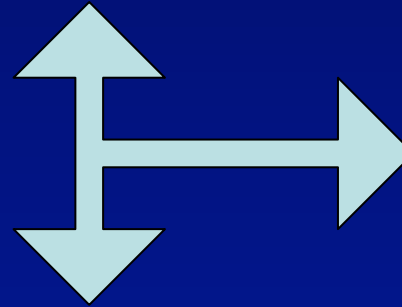
Inflammation

- Obesity
- Process sugar
- Smoking
- inflammatory foods

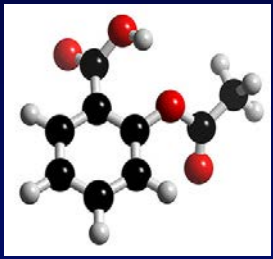


Anti-inflammation

- Exercise
- Nuts & legumes
- Healthy bacteria
- Polyphenols



- Cancer
- Cancer growth
- Fatigue
- Irritable bowel
- Low mood
- Depression
- Arthritis
- Diabetes
- Cholesterol
- Heart disease
- hypertension
- Dementia
- Parkinson's

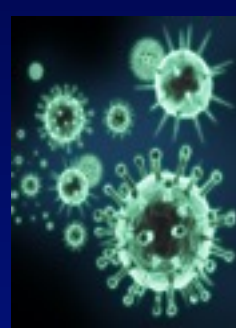


Biochemical changes

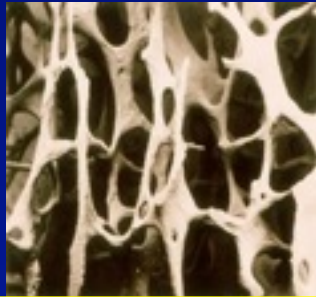
- Oestrogen levels
- Insulin Like growth factors
- Insulin Sensitivity
- Epigenetic gene expression
- Vasoactive Intestinal Protein
- Leptin
- Irisin



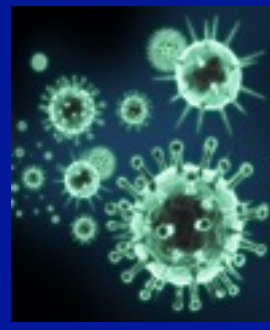
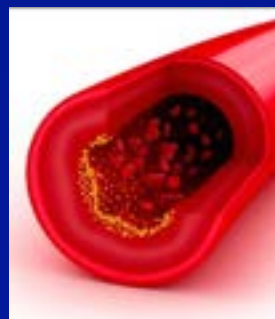
Chemotherapy



Hormonal drugs



Biological agents



Meta analysis of 33 RCT studying exercise interventions after cancer

- Fatigue and tiredness
- Mood, anxiety & depression
- Muscle power
- Exercise capacity
- Distance walked in 5 minutes
- Overall Quality of life

Fong J, Hong Kong & Liam Bourke L, Barts *BMJ* 2012; 344:



Appropriate exercises

Weight reduction

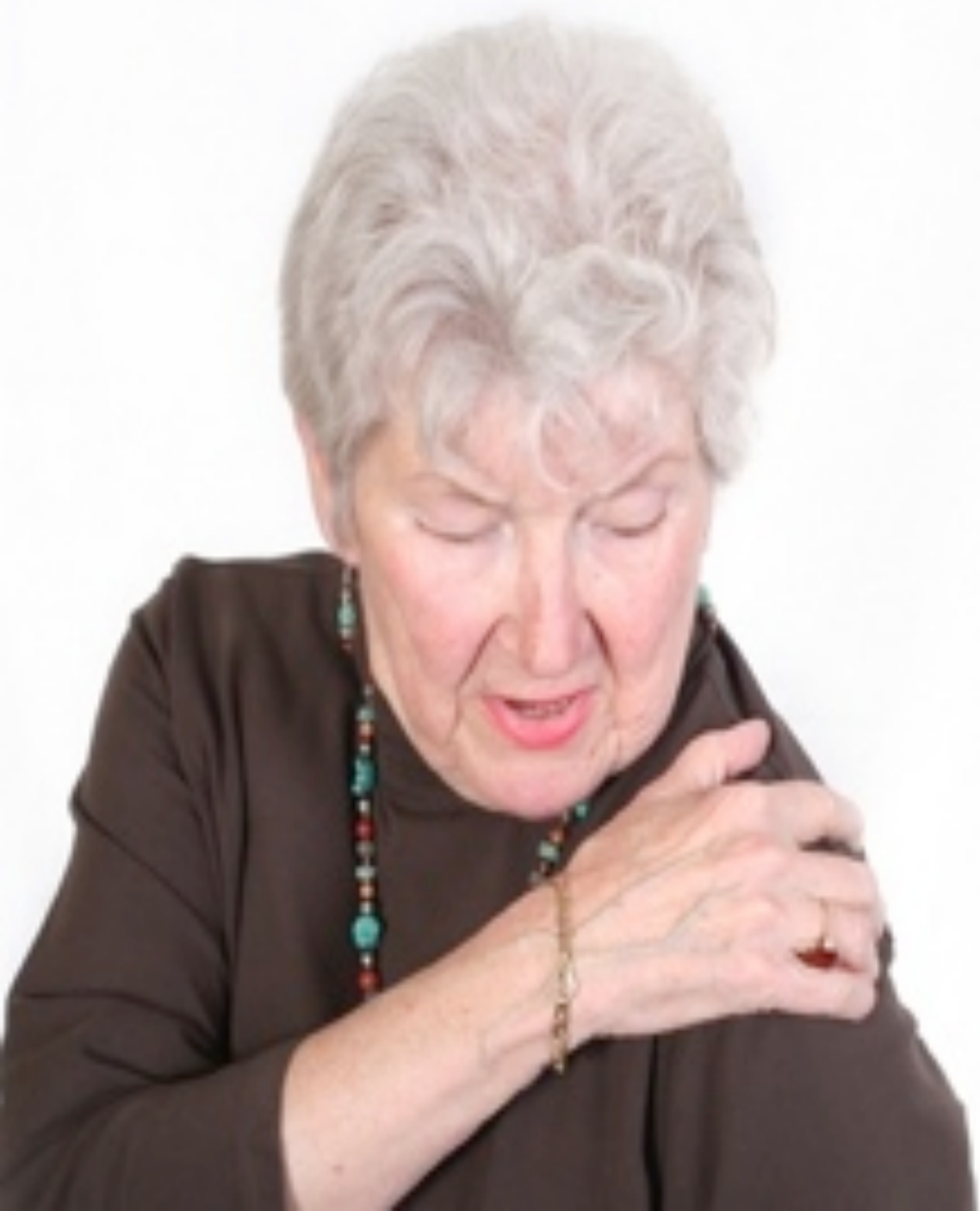


Stress



Osteoporosis





Arthralgia incidence

55% of breast cancer*

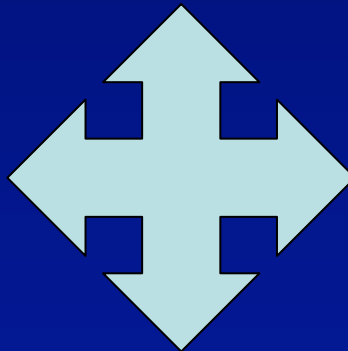
40% prostate cancer survivors*

- Osteoarthritis
- Chemotherapy (Taxotere)
- Tamoxifen
- Aromatase inhibitors
- Herceptin and other biologicals

* Younger age

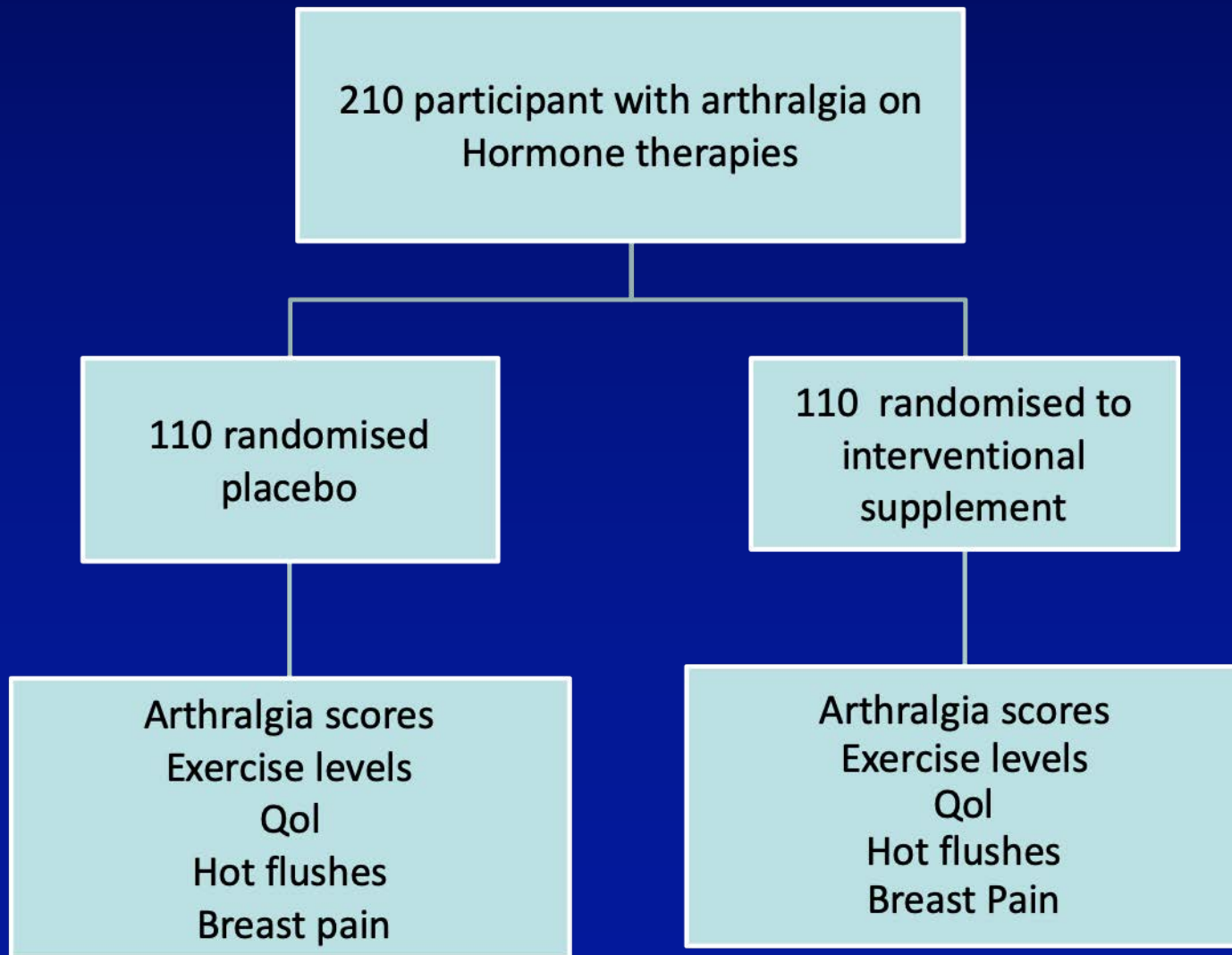


Barrier to exercise is arthralgia



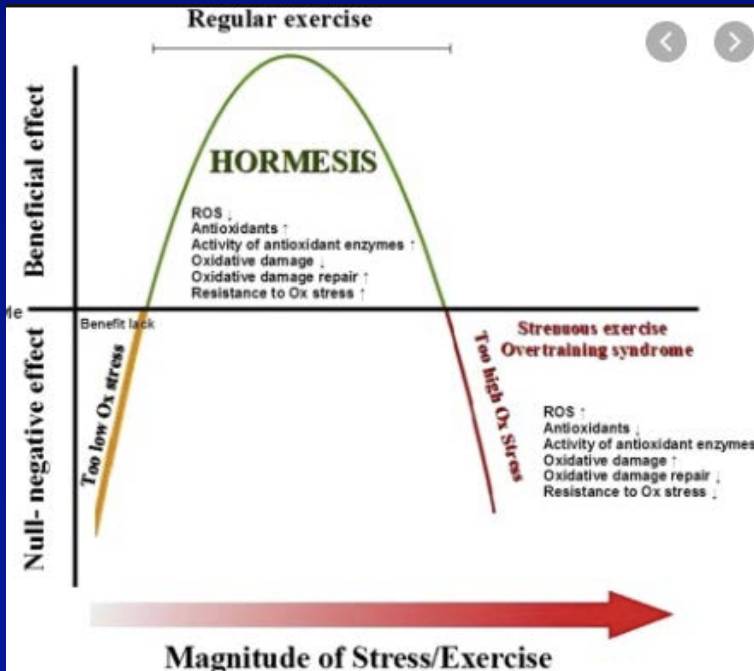
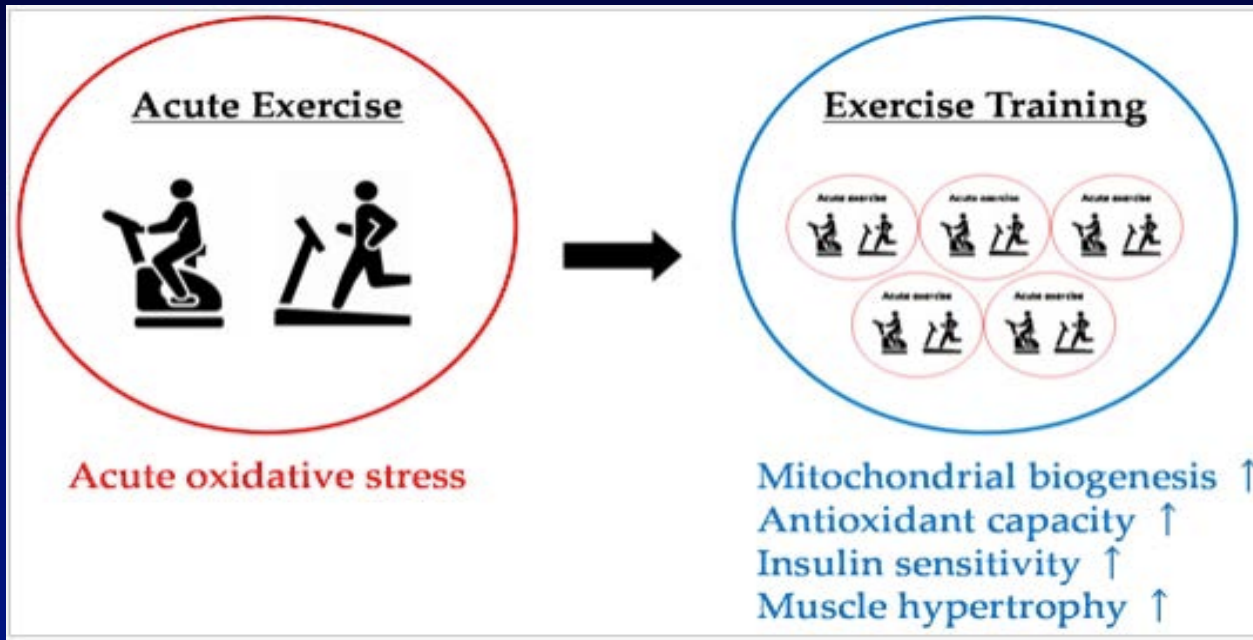


A double blind RCT of a phytochemical rich supplement for hormonal induced arthralgia (EudraCT 2015-002018-66)



Risks





- Transient increase in ROS
- Adaptive process
- Increases antioxidant enzymes
- So a long term antioxidant
- Adequate mineral intake
- Adequate polyphenol intake.

Gomez-Cabrera. Free R. Biol Med 2008 15;44(2):126
 Ji LL. Ann NY Acad Sci. 2001; 928:236-47.2001
 Kojda. Cardiovascular research. 2005;67:187
 Pirgitore Nutrition Vol 31 (7-8), p 916

Exercise increase ROS

By-product of cellular energy production

Polyphenol / nitrate rich diet / supplements:

- Turmeric | Green Tea | Beetroot |
- Broccoli | Cordesvpes | Pomegranate

Adaptive increase in anti-oxidative enzymes

Better performance

- Better muscle recovery
- Joint protection
- Better gut health



Long term lower oxidative stress



Direct anti-oxidant vitamins

- Vitamin A
- Vitamin E

Block antioxidant adaption

Long term greater oxidative stress



Poor performance



Polyphenol rich foods



~~Not direct anti-oxidants~~

Enhance anti-oxidant enzyme capacity
via Nrf-2 efficiency and other cytoprotective phase 2 enzymes

- SOD
- Gluathione
- Catalase

Inflammatory regulation:

- Cox-2 and 5- Lox
- Nf-KappaB
 - Genetic transcription factor for innate immunity
 - Cytokines, chemokines, adhesion molecules

Epigenetic expression

- Promote tumour suppressor genes
- Inhibit cancer promotor genes

Improve gut health

- Pre-biotics
- Interfere with firmicute (inflammatory) growth

Diabetic protection

- Slow Glycaemic index
- Increase insulin sensitivity

Direct cancer proliferation inhibition

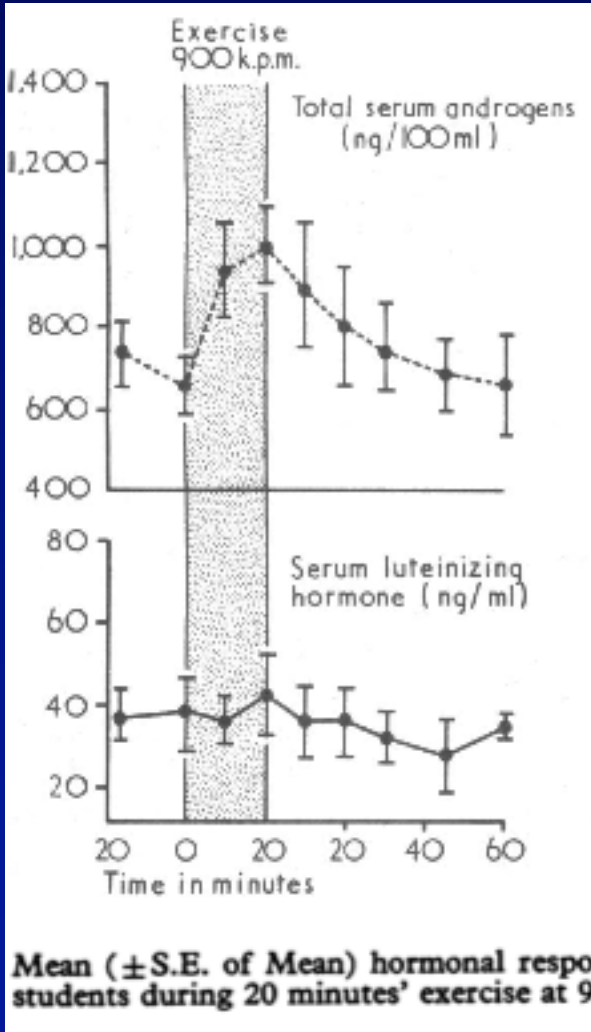
- HER2
- PARP
- BCL-s

Improve DNA repair

- Upregulate BRCa 1
- Upregulate p53



Testosterone



- Short lived
- Total not free testosterone increases
- This effect not seen in over 55 years
- Levels fall with regular training

Kaaks. *Ann NY Acad Sci* 2002; 963: 268-281.

Hayes *Aging Male* 2015, 18(3):195-200

Sutton *BMJ* 1973, 1, 520-22

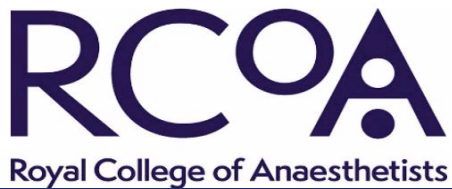
Safarinejad *Endocrinol* 2009 ;200(3):259-71

Craig Mech *Ageing Dev.* 1989 49(2):159-69.

When to start?



Prehabilitation



WE ARE
MACMILLAN.
CANCER SUPPORT

NIHR

National Institute
for Health Research

UK consensus on exercise guided prehabilitation

- Reduce thrombotic events
- Reduce time in hospital
- Reduce readmission rates
- Research questions:
 - Reduce relapse
 - Improve survival



Androgen deprivation therapy



121 men with Ca P starting ADT

Resistance and aerobic exercise programme better:

- Muscle strength
- BMI
- Abdominal fat, triglycerides, blood sugar (Metabolic syndrome)



ELSEVIER

Lifestyle Factors Correlate with the Risk of Late Pelvic Symptoms after Prostatic Radiotherapy

R.J. Thomas^{*†‡}, M. Holm[§], M. Williams^{*}, E. Bowman[¶], P. Bellamy[‡], J. Andreyev^{||}, J. Maher[¶]

journal homepage: www.clinicaloncologyonline.net



440 men with prostate cancer treated over 10 years

	Exercise	Smokers	Age	BMI
Rectal toxicity	✓	✓	NS	✓
Incontinence	✓	✓	NS	NS
Erectile function	✓	NS	NS	NS





PACES RCT during chemotherapy

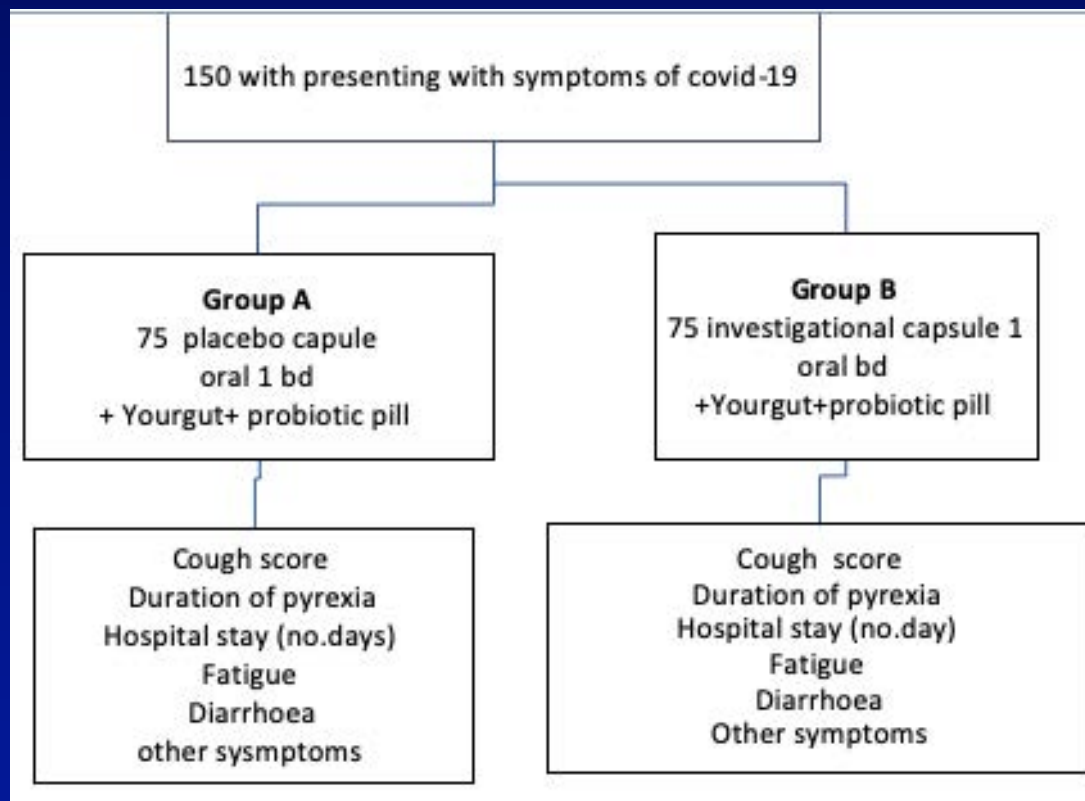
- 230 women receiving chemotherapy
- Supervised High intensity v Home based v standard
- HI & HB >standard but HI > HB:
- Less decline in cardiorespiratory fitness ($P < .001$),
- Better physical functioning ($P \leq .001$),
- Less nausea and vomiting ($P = .029$)
- Less pain ($P = .003$),
- Better muscle strength ($P = .002$)
- Less fatigue ($P < .001$)

A randomised double blind placebo controlled trial evaluating the influence of **phytochemical** rich foods capsule plus or minus a probiotic capsule on clinical outcomes among individuals with covid-19 viral infection
(The UK Phyto-V Study)



The UK Covid-19 nutritional intervention study

The UK Phyto-V study



Exercise
advice

Exercise
advice



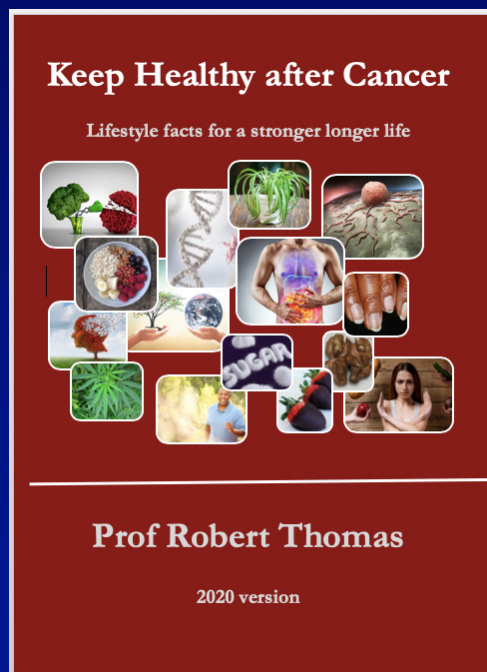
<http://Phyto-v.com>

Madeleine.Williams@bedfordhospital.nhs.uk

Conclusion

- Strong evidence for wellbeing
- Reasonable evidence for outcomes
- Feasible biological mechanisms of action
- Start early aim for 3-5 hours / week
- Safe
- Role for linked targeted nutritional strategies
- We need to try harder to motivate patients

More information



Appendix to Talk

Cancer incidence & physical activity



- Uterus - Voskuil et al, *Cancer Epi Biomarkers Prev* 2007;16:639-48.
- Colon - Boyle et al *J Natl Cancer Inst* 2012;104:1548-1561.
- Bladder - Keimling et al. *Br J Cancer* 2014;110:1862-1870.
- Renal - Behrens et al. *Br J Cancer* 2013;108:798-811
- Breast - Wu et al *Breast Cancer Res Treat.* 2013;137:869–82.
- Prostate - Kenfield et al *J Natl Cancer Inst* 2016;108(3)
- Lung - Tardon et al *Cancer Causes Control.* 2005, 16(4): 389–39
- Breast - Thune et al *N Engl J Med* 1997;1(336):1269-1275.



Exercise after bowel cancer

- Melbourne Collaborative cohort study**, 526 patients with ca colon. At 5 years:
- 57% alive (non-exercisers) v 71% alive (1-2 sports/wk)

Haydon 2006

- Intergroup CALGB 89803 study**, stage III:

- 35% overall survival difference upper to lower quartiles of activity

Meyerhardt 2005;

- Health Professional Follow up study (USA)**

- Lower cancer specific mortality >27 v < 3 METS per week

Meyerhardt 2009

- NIH–AARP Diet and Health Study**

- 31% overall survival LTPA ≥ 7 h/wk (TV watching linked with mortality)

Arem JCO 2014



Exercise after breast cancer

- 933 BC survivors PE > 2.5 hrs/week 67% reduction in RR
Irwin M et al 2007 JCO
- 4482 BC survivors PE > 2.8 hrs/wk 35-49% reduction in RR
Holick C et al 2008
- 1879 women, The LACE study OS better upper versus lower quarter
Sternfeld et al (2009)
- 2987 women Nurses Health study 3-5 hrs/wk better OS and RR
Holmes et al JAMA 2005
- 1490 BC 30 mins 6 days a wk (+ >5 fruit/veg a day) greater survival
Pierce et al 2007 JCO
- 4826 women, The Shanghai Cancer Registry; 8 MET/wk v sedentary
Chen et al 2001



Exercise after Prostate cancer

- Health Professionals Follow-Up Study (2705). Physical Activity and Survival after Prostate Cancer.

Kenfield et al. JCO 2011

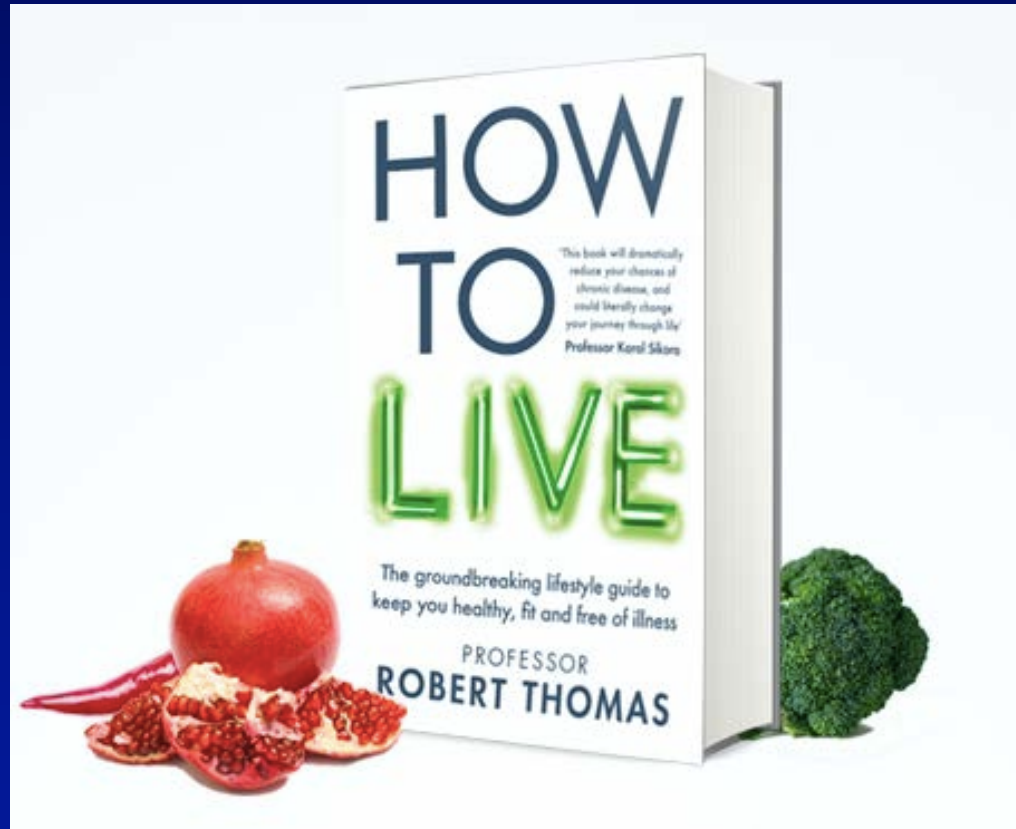
- Physical Activity and Risk of Prostate Cancer Progression: Prostate Strategic Urologic Research Endeavour.

Richman et al. Can Res 2011

- Health professionals Follow up study – fatal prostate cancers lower in men who exercised over the age of 65 years

Giovanucci et al Arch Intern Med. 2005

More information



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