

Professor Robert Thomas

Macmillan Consultant Oncologist, Cranfield University
Bedford and Addenbrooke's Hospitals

Elizabeth Butler

Nutritional therapist
Penny Brohn Cancer Care

Essential micro nutrient testing – pros and cons.

Many cancer survivors are turning to nutritional testing in order to empower themselves with the knowledge to make optimal lifestyle choices based on their individual profile. Although popular for sports professionals, what are the advantages for those with cancer who wish to follow a diet that supports their health and is this money well spent?

What is micro nutrient testing?

Although not all the same, these tests are fundamentally a measure of the body's essential micro nutrients, usually taken from a blood test but can be from urine, sweat, hair, saliva or even toe nail clippings! A vast array of nutrients can be analysed but the most important and relevant have been collated in the recently developed *Cancer Risk Nutritional Profile*. This includes 50 of the body's chemicals which, either in excess or deficiency, have been involved in the cancer promotion pathways. They include the following categories:

- Fat soluble vitamins
- Water soluble vitamins
- Essential minerals
- Essential fatty acids
- Omega 3 (long and short chain)
- Omega 6 and 9 fatty acids
- The ratio of omega 3:6
- Antioxidant levels
- Antioxidant enzymes.

Why are micronutrients important in the cancer process?

Vitamins, essential mineral and fatty acids cannot be made by the body so have to be eaten except Vitamin D which is largely generated by sunlight on the skin. They are crucial components of enzymes, and chemicals required for metabolism and efficient day to day function of the body. Although, in Western society, gross deficiency diseases such as scurvy, beri beri and pellagra are rare, minor deficiencies may develop that can cause imbalances in the regulatory and immunogenic processes.

Copper, zinc, selenium and manganese are all required to make the three main antioxidant enzymes catalase, glutathione S-transferase glutathione; superoxide dismutase. Deficiencies in these have been shown to reduce the ability to mop up free radicals generated by environmental and dietary carcinogens. A study from China, for example, gave selenium to the inhabitants of one of two villages both known to have low selenium in the food chain. At 2 years, the risk of liver cancer had substantially reduced in the village which received selenium supplementation.

Vitamin A added to cancer cells slows growth rates and increased apoptosis. A study from California showed that cells deficient in the B vitamins (B12, folate, niacin) sustained DNA damage similar to that seen after carcinogenic exposure. Vitamin C is involved in the mechanism which enables DNA to 'sense' the damage done by free radicals, by integrating with the iron imbedded in DNA. This process facilitates DNA repair and is therefore a significant aspect of immune surveillance. Vitamin D has been shown to reduce proliferation, promote differentiation, inhibit invasion, angiogenesis, prevent loss of adhesion, promote apoptosis. Clinical studies have shown that those survivors of bowel and breast cancer with regular exposure to sunlight had a lower incidence of subsequent relapse. Vitamin E has direct antioxidant effects and prevents cancer cells de-differentiating into more aggressive forms. A study from Finland showed that people with higher serum vitamin E levels had a low risk of bowel cancer.

Omega 3, are not made by the body so also have to be eaten. They are essential for the formation of hormones, particularly those involved in inflammation and immunity (e.g. prostaglandins, leukotrienes, thromboxanes). They have COX-2 inhibition properties which in turn has direct anticancer properties. In USA Health professionals Study men who had the highest intake of omega 3 had they lowest incidence of aggressive prostate cancer. The long chain omega-3's, Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA), are particularly healthy and these can be made in the body from the short chain omega-3, Alpha-linolenic acid (LLA). Omega-6 however block this process so the ratio of omega 3:6 is important. Ideally it should be 1:2 or 1:3 but in most western societies the ratio are generally much higher as omega-3 have been removed from our food chain via intensive meat farming and fast foods. Laboratory experiments have also demonstrated that oleic acid helps repair DNA damage caused by excessive sunlight. Olive oil has been shown to suppress over-expressed Her-2 protein on breast cancer cells.

Why not simply take additional micronutrient supplements?

At first sight it would seem obvious to boost the body's nutrients with one of the many commercially available supplements – job done and no need to worry! Alas, the human body is not that easy, there is also plenty of good evidence to show that micronutrient excess can also cause harm, not only in terms of cancer but other serious diseases and long term supplement intake can risk excessive levels. Some more notable examples are summarised here:

The large international SELECT study of selenium and zinc supplementation did not show any benefit in prostate cancer risk and there was a trend towards more aggressive

cancers in the selenium group. In the health professional study men who took zinc supplementation over long periods of time actually had a higher risk of prostate cancer.

A study of vitamin A supplements involving 30,000 male smokers, found that there was a reduction in the incidence of prostate cancer, but the incidence of lung cancer was actually higher. A substantial European study gave vitamin E in the form of alpha-tocopherol and Vitamin A supplements in the form of beta carotene to individuals who were either heavy smokers, or who had previously had cancer of the throat. The trial showed an elevated risk of both lung and prostate cancer and a higher rate of cerebral haemorrhage if they also had high blood pressure.

A study from Norway gave vitamin B supplements or placebo to patients with angina or following a heart attack in an attempt to reduce the incidence of another cardiac event. After three years there was no cardiac benefit but a significant increase in cancer. These results were confirmed in a separate post heart-attack study also published in 2009. Men who took folic acid supplements were more than twice as likely to develop prostate cancer compared with men who took a placebo. This study made another interesting observation: it also found that, independent to whether they took a supplement or not, the prostate cancer incidence was slightly lower in men who had adequate amounts of folate in their diet.

A study from Queensland Australia analysed over a thousand individuals who had been treated for skin cancer. The risk of a further cancer was reduced if individuals ate foods with a high level of dietary antioxidants compared to those who did not, but individuals who took supplements of vitamin E actually had a higher rate of recurrent skin cancers. A further study which supplemented women with alpha-tocopherol, demonstrated no reduction in cancer, but the incidence of heart disease was slightly worse.

Another large human dietary prevention study combined beta-carotene and retinal analogues of vitamin A. People at the start of this study had their serum vitamin A levels measured but all took the same interventional supplement dose. Those participants who started the trial with naturally low blood levels of beta-carotene had lower levels of prostate cancer after years of supplementation. Those people who had adequate blood levels at the start of the study ended up with a higher risk of cancer, particularly prostate. This trial provides a clear take home message, that correcting a natural or acquired deficit is beneficial, but too much is harmful.

What do these data suggest?

- If there is an essential micronutrient deficiency the risk of cancer increases
- If there is an excess or likely excess caused by uncontrolled supplementation intake the risk of cancer increases

What are the chances of a micronutrient imbalance after cancer?

Various studies have reported deficiencies among patients after cancer particularly with Vitamin D in the region of 40-60%. Since we started the *cancer risk nutritional profile* service we have also seen Vitamin D levels below normal in over 75% of cases. The most common deficiencies, however, are omega 3, particularly the important long chain varieties. Over 50% so far have also had a mineral deficiency or excess (Particularly zinc and

selenium) but no clear pattern has emerged. The ratios of omega 3:6 are consistently greater than 1:5 with some above 1:10. Lycopene and lutein levels have been sub optimal in all but one of the men with prostate cancer.

What are “Cons” of nutritional testing?

The tests are not cheap, they are not usually available on the NHS and most private policies do not cover them. Nevertheless, as the advice provided in the reports aims to restore nutritional harmony with diet and not additional supplements then, in the long term, there is likely to be savings. Secondly, they are snap shot in time, generally reflecting the previous few weeks dietary pattern or even shorter for vitamin C. Provided there has not been a major change in lifestyle over this time, however, they are likely to represent a more global picture but it is advisable to have the test done at a time which reflects the usually day to day pattern as much as possible (e.g. not immediately after a holiday or major illness).

Conclusions

Published data strongly suggests that micronutrient imbalance is a risk for cancer. It also suggests that restoring nutritional harmony reduces the risk, although randomised controlled trials are clearly needed. Whether this applies after cancer, to reduce the risk of relapse and improve well-being, remains unproven but the assumption is that factors which cause cancer in the first place are usually detrimental afterwards. As an alternative to blind, often costly supplement intake, the Cancer Risk Nutritional profile has the advantage of empowering individuals with specific advice relevant to their own make up.

How to order “The Cancer Risk Profile”: See Cancernet.co.uk/nutritional-tests.htm

References

1. [Ades PA](#), [Huang D](#), [Weaver SO](#) (1992) Cardiac rehabilitation participation predicts lower rehospitalization costs. [Am Heart J](#). 1992 Apr; 123(4 Pt 1):916-21.
2. Adlercreutz H, Fotsis T, and e.a. Bannwart C (1986) Urinary estrogen profile determination in young Finnish vegetarian and omnivorous women. [J Steroid Biochem](#). 24: p. 289-95.
3. Allen, N. E., V. Beral, et al. (2009). "Moderate Alcohol Intake and Cancer Incidence in Women." [J. Natl. Cancer Inst](#). 101(5): 296-305.
4. Amling C, [Riffenburgh RH](#), [Sun L](#), [Moul JW](#), [Lance RS](#), [Kusuda L](#), [Sexton WJ](#), [Soderdahl DW](#), [Donahue TF](#), [Foley JP](#), [Chung AK](#), [McLeod DG](#). (2004) Pathologic variables and recurrence rates as related to obesity and race in men with prostate cancer undergoing radical prostatectomy. [J Clin Oncol](#)., 22: p. 439-445.
5. Augustsson K, [Michaud DS](#), [Rimm EB](#), [Leitzmann MF](#), [Stampfer MJ](#), [Willett WC](#), [Giovannucci E](#). (2003) A prospective study of intake of fish and marine fatty acids and prostate cancer. [Cancer Epidemiol Biomarkers Prevent](#), 12: p. 64-67.

6. Baron JA, [Cole BF](#), [Sandler RS](#), [Haile RW](#), [Ahnen D](#), [Bresalier R](#), [McKeown-Eyssen G](#), [Summers RW](#), [Rothstein R](#), [Burke CA](#), [Snover DC](#), [Church TR](#), [Allen JI](#), [Beach M](#), [Beck GJ](#), [Bond JH](#), [Byers T](#), [Greenberg ER](#), [Mandel JS](#), [Marcon N](#), [Mott LA](#), [Pearson L](#), [Saibil F](#), [van Stolk RU](#). (2003) A randomised trial of aspirin to prevent colorectal adenomas. *The New England Journal of Medicine*, 348(10): p. 891-899.
7. Battaglini C. (2004) A randomized study on the effects of a prescribed exercise intervention on lean mass and fatigue changes in breast cancer patients during treatment. Dissertation: http://gateway.proquest.com/openurl%3furl_ver=Z39.88-2004%26res_dat=xri:pqdiss%26rft_val_fmt=info:ofi/fmt:kev:mtx:dissertation%26rft_dat=xri:pqdiss:3139617
8. Baxter RC and Turtle JR (1978) Regulation of hepatic growth hormone receptors by insulin. *Biochem Biophys Res Commun*, 84: p. 350-7.
9. Berwick M, Armstrong BK, Ben-Porat L, Fine J, Kricker A, Eberle C, Barnhill R. Sun exposure and mortality from melanoma. *J Natl Cancer Inst* 2005;97:195-9.
10. Blacklock CJ, Lawrence JR, Wiles D, Malcolm EA, Gibson IH, Kelly CJ, Paterson JR (2001) Salicylic acid in the serum of subjects not taking aspirin. Comparison of salicylic acid concentrations in the serum of vegetarians, non-vegetarians, and patients taking low dose aspirin. *Journal of Clinical Pathology*, 54: p. 553-555.
11. Blot WJ, Li J, Taylor PR, Guo W, Dawsey S, Wang GQ, Yang CS, Zheng SF, Gail M, Li GY, Liu BQ, Tangrea J, Sun YH, Liu F, Fraumeni JF, Zhang YH, Li B. (1993) Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J. Natl. Cancer Inst. (Bethesda)*, 85: 1483-1492.
12. Blutt SE, [McDonnell TJ](#), [Polek TC](#), [Weigel NL](#). (2000) Calcitriol-induced apoptosis in LNCaP cells is blocked by overexpression of bcl-2. *Endocrinology*, 141: p. 10-17.
13. Campbell A, Mutrie N, White F, McGuire F, Kearney N. (2005) A pilot study of a supervised group exercise programme as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment. *Eur.J.Oncol.Nurs*; 9:56-63.
14. Campell MJ, Koeffler HP (1997) Toward therapeutic intervention of cancer by vitamin D compounds. *J Natl Cancer Inst*, 89: p. 182-185.
15. Chan JM, Gann PH, and Giovannucci EL (2005) Role of diet in prostate cancer development and progression. *Journal of Clinical Oncology*, 23(32): p. 8152-60.
16. Chang PH, Lai YH, Shun SC et al. (2008) Effects of a walking intervention on fatigue-related experiences of hospitalized acute myelogenous leukemia patients undergoing chemotherapy: a randomized controlled trial. *J Pain Symptom.Manage*;35:524-
17. Chaudry AA, Wahle KWJ, McClinton S, Moffat LEF (1994) Arachidonic acid metabolism in benign and malignant prostatic tissue in vitro: Effects of fatty acids and cyclooxygenase inhibitors. *Int J Cancer*, 57: p. 176-180.

18. Chen L, [Stacewicz-Sapuntzakis M](#), [Duncan C](#), [Sharifi R](#), [Ghosh L](#), [van Breemen R](#), [Ashton D](#), [Bowen PE](#). (2001) Oxidative DNA damage in prostate cancer patients consuming tomato sauce-based entrees as a whole-food intervention. *J Natl Cancer Inst*, 93: p. 1872-1879.
19. Cheng, M (2009) Tanning beds are as deadly as arsenic, cancer study says. http://www.boston.com/news/nation/articles/2009/07/29/cancer_study_shows_tanning_beds_as_deadly_as_arsenic/.
20. Chlebowski R, Aiello E, and McTiernan A. (2002) Weight loss in breast cancer patient management. *J Clin Oncol.*, 20: p. 1128-1143.
21. Chlebowski RT, Blackburn GL, Elashoff RE, Thomson C, Goodman MT, Shapiro A, Giuliano AE, Karanja N, Hoy MK, Nixon DW and The WINS Investigators (2005) Dietary fat reduction in post menopausal women with primary breast cancer. *Journal of Clinical Oncology*, (10): p. 3s.
22. Clark LC, [Dalkin B](#), [Krongrad A](#), [Combs GF Jr](#), [Turnbull BW](#), [Slate EH](#), [Witherington R](#), [Herlong JH](#), [Janosko E](#), [Carpenter D](#), [Borosso C](#), [Falk S](#), [Rounder J](#). (1998) Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial. *British Journal of Urology*, 81: p. 730-734.
23. Coleman EA, Coon S, Hall-Barrow J, Richards K, Gaylor D, Stewart B. (2003) Feasibility of exercise during treatment for multiple myeloma. *Cancer Nurs*;26:410-419.
24. Coombs GF (2004) Status of selenium in prostate cancer prevention. *British Journal of Cancer*, 91: p. 195-199.
25. Courneya KS, Segal RJ, Mackey JR et al. (2007) Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. *J.Clin.Oncol*;25:4396-4404.
26. Courneya KS, Segal RJ, Gelmon K et al. (2007) Six-month follow-up of patient-rated outcomes in a randomized controlled trial of exercise training during breast cancer chemotherapy. *Cancer Epidemiol.Biomarkers Prev.*;16:2572-2578.
27. Cramp F, Daniel J. (2008) Exercise for the management of cancer-related fatigue in adults. *Cochrane.Database.Syst.Rev.* 2008;CD006145
28. Crowley S. (2003) The effect of a structured exercise program on fatigue, strength, endurance, physical self-efficacy, and functional wellness in women with early stage breast cancer;127.

29. Davies, N.J., Kinman, G., Thomas, R.J., and Bailey, T.A. (2008) Information satisfaction in breast and prostate cancer patients: Implications for quality of life. *Psycho-Oncology*, published online at <http://www3.interscience.wiley.com/cgi-bin/abstract/117871474/ABSTRACT>.
30. Demark-Wahnefried W, Aziz NM, Rowland JH, Pinto BM (2005) Riding the Crest of the Teachable Moment: Promoting Long-Term Health After the Diagnosis of Cancer *Journal of Clinical Oncology*, Vol 23, No 24 (August 20), pp. 5814-5830.
31. Dieppe P, Ebrahim S, and Juni P (2004) Lessons from the withdrawal from rofecoxib. *BMJ*, 329: p. 867-868.
32. Dignam JJ, Polite B, Yothers G, Raich P, Colangelo L, O'Connell M and Wolmark N (2006) Effect of body mass index on outcome in patients with dukes B and C colon cancer: An analysis of NSABP trials. *Journal of Clinical Oncology*, 3533: p. 254s.
33. Dignam, J. J., B. N. Polite, et al. (2006). "Body Mass Index and Outcomes in Patients Who Receive Adjuvant Chemotherapy for Colon Cancer." *J. Natl. Cancer Inst.* 98(22): 1647-1654.
34. Drouin J, Krause S, Orr J. (2005) Effects of aerobic exercise training on Peak Aerobic Capacity, Fatigue, and Psychological factors during radiation for breast cancer. *Rehabilitation Oncology*;23:11-17.
35. Ebbing M, Bønaa, KH, Nygård O, Arnesen E, Ueland PM, Nordrehaug JE, Rasmussen K, Njølstad I, Refsum H, Nilsen DW, Tverdal A, Meyer K, Vollset SE (2009) Cancer Incidence and Mortality After Treatment With Folic Acid and Vitamin B12 *JAMA*. 2009;302(19):2119-2126.
36. Egan KM, Stampfer MJ, Giovannucci E, Rosner BA, Colditz GA (1996) Prospective study of regular aspirin use and the risk of breast cancer. *Journal of the National Cancer Institute*, 88: p. 988-993.
37. Evans BA, Griffiths K, and Morton MS (1995) Inhibition of 5 alpha-reductase in genital skin fibroblasts and prostate tissue by dietary lignans and isoflavonoids. *Journal of Endocrinology*, 147: p. 295-302.
38. Figueiredo, J. C., M. V. Grau, et al. (2009). "Folic Acid and Risk of Prostate Cancer: Results From a Randomized Clinical Trial." *J. Natl. Cancer Inst.* 101(6): 432-435.
39. Flowers, M. and P. A. Thompson (2009). Conjugated Linoleic Acid Suppresses HER2 Protein and Enhances Apoptosis in SKBr3 Breast Cancer Cells: Possible Role of COX2." *PLoS ONE* 4(4): e5342.

40. Food and Drug Administration (FDA) (2006) Carcinogens and antioxidants.
41. Fraga CU (1991) Ascorbic acid protects against endogenous oxidative DNA damage in human sperm. *Proc Natl Acad Sci USA*, 88(24): p. 11003.
42. [Friedenreich CM, et al "Alberta physical activity and breast cancer prevention trial: Sex hormone changes in a year-long exercise intervention among postmenopausal women" *J Clin Oncol* 2010; DOI: 10.1200/JCO.2009.24.9557.](#)
43. Freier S, [Weiss O](#), [Eran M](#), [Flyvbjerg A](#), [Dahan R](#), [Nephesh I](#), [Safra T](#), [Shiloni E](#), [Raz I](#). (1999) Expression of the insulin-like growth factors and their receptors in adenocarcinoma of the colon. *Gut*, 44: p. 704-8.
44. Fuchs C, Meyerhardt JA, Heseltine DL, Niedzwiecki D, Hollis D, Chan AT, Saltz LB, Schilsky RL and Mayer RJ (2005) Influence of regular aspirin use on survival for patients with stage III colon cancer: Findings from intergroup trial CALGB 89803. American Society of Clinical Oncology Abstract Book, 2005.
45. Giles GG and English DR (2002) The Melbourne Collaborative Cohort Study. *IARC Sci Publ*, 156: p. 69-70.
46. Giovannucci E, [Rimm EB](#), [Liu Y](#), [Stampfer MJ](#), [Willett WC](#). (2002) A prospective study of tomato products, lycopene, and prostate cancer risk. *Journal of the National Cancer Institute*, 94: p. 391-398.
47. Gold EB, Pierce JP, Natarajan L, Stefanick ML, Laughlin GA, Caan BJ, Flatt SW, Emond JA, Saquib N, Madlensky L, Kealey S, Wasserman L, Thomson CA, Rock CL, Parker BA, Karanja N, Jones V, Hajek RA, Pu M, and Mortimer JE. (2009) Dietary Pattern Influences Breast Cancer Prognosis in Women Without Hot Flashes: *JCO* vol 27, no.3; 352-359.
48. Golden, E. B., P. Y. Lam, et al. (2009). "Green tea polyphenols block the anticancer effects of bortezomib and other boronic acid-based proteasome inhibitors." *Blood* 113(23): 5927-5937.
49. Gong, Z., A. R. Kristal, et al. (2009). "Alcohol consumption, finasteride, and prostate cancer risk." *Cancer* 115(16): 3661-3669.
50. Goodwin PJ, Ennis M, Pritchard KI, Koo J, Hood N (2009) Prognostic Effects of 25-Hydroxyvitamin D Levels in Early Breast Cancer. *Journal of Clinical Oncology*, Vol 27, No 23 (August 10): pp. 3757-3763.

51. Gritz ER (1993) Cancer Smoking Epidemiology Biomarkers & Prevention, 2;(3); 261-270.
52. Gross M, Jo S, Huang D, Mirocha J, Shazer R, Holden S and Agus D (2006) Obesity, ethnicity and surgical outcome for clinically localized prostate cancer. Journal of Clinical Oncology, 5(9615 supplement): p. 865.
53. Hamilton M, Wolf J, Rusk J (2006) Effects of Smoking on the Pharmacokinetics of Erlotinib. Clinical Cancer Research doi: 10.1158/1078-0432.CCR-05-2235 Clinical Cancer Research April 1, 12, 2166.
54. Harris RE, Namboodiri KK, and Farrar WB. (1996) Nonsteroidal antiinflammatory drugs and breast cancer. Epidemiology, 7: p. 203-205.
55. Harvei S, [Bjerve KS](#), [Tretli S](#), [Jellum E](#), [Robsahm TE](#), [Vatten L](#). (1997) Prediagnostic level of fatty acids in serum phospholipids: Omega-3 and omega-6 fatty acids and the risk of prostate cancer. Int J Cancer, 71(545-551).
56. Hayes SC, Spence RR, Galvao DA, Newton RU (2009) Australian Association for Exercise and Sport Science position stand: Optimising cancer outcomes through exercise. J.Sci.Med.Sport. 2009;12:428-434.
57. Haydon AM, [Macinnis RJ](#), [English DR](#), [Giles GG](#). (2006) The effect of physical activity and body size on survival after diagnosis with colorectal cancer. Gut, 55: p. 62-67.
58. Headley JA, Ownby KK, John LD. (2004) The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. Oncol.Nurs.Forum; 31:977-983.
59. Heinen et al (2007) Antioxidant intake and skin cancer relapse. EJC 200, 2707-16
60. Heinonen OP, [Albanes D](#), [Virtamo J](#), [Taylor PR](#), [Huttunen JK](#), [Hartman AM](#), [Haapakoski J](#), [Malila N](#), [Rautalahti M](#), [Ripatti S](#), [Mäenpää H](#), [Teerenhovi L](#), [Koss L](#), [Virolainen M](#), [Edwards BK](#). (1998) Prostate cancer and supplementation with alpha-tocopherol and beta carotene: Incidence and mortality in a controlled trial. J Natl Cancer Inst, 90: p. 440-446.
61. Hippisley-Cox J and Coupland C (2005) Risk of myocardial infarction in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. British Medical Journal, 330: p. 1366-1369.
62. Holick CN, Newcomb PA, Trentham-Dietz A, Titus-Ernstoff L, Bersch AJ, Stampfer MJ, Baron JA, Egan KM, and Willett WC (2008)

Physical Activity and Survival after Diagnosis of Invasive Breast Cancer. *Cancer Epidemiological Biomarkers Prev.*, PP. 379-386.

63. Holmes MD, [Stampfer MJ](#), [Colditz GA](#), [Rosner B](#), [Hunter DJ](#), [Willett WC](#). (1999) Dietary factors and the survival of women with breast cancer. *Cancer*, 85(5): p. 826-35.
64. Holmes MD, [Chen WY](#), [Feskanich D](#), [Kroenke CH](#), [Colditz GA](#). (2005) Physical activity and survival after breast cancer diagnosis. *JAMA*, 293: p. 2479-86.
65. Hsieh T and Wu JM, (1997) Induction of apoptosis and altered nuclear/cytoplasmic distribution of the androgen receptor and prostate-specific antigen by 1 alpha, 25-dihydroxyvitamin D3 in androgen-responsive LNCaP cells. *Biochemical and biophysical research communications*, 235: p. 539-544.
66. Hsu AL, Ching Tt, Wang DS, Song X, Rangnekar VM, Chen CS (2000) The cyclooxygenases-2 inhibitor celecoxib induces apoptosis by blocking Akt activation in human prostate cancer cells independently of Bcl-2. *Journal of Biological Chemistry*, 275: p. 11397-11403.
67. Hwang JH, Chang HJ, Shim YH et al.(2008) Effects of supervised exercise therapy in patients receiving radiotherapy for breast cancer. *Yonsei Med.J.*;49:443-450.
68. Jackson MJ, [Dillon SA](#), [Broome CS](#), [McArdle A](#), [Hart CA](#), [McArdle F](#). (2004) Are there functional consequences of a reduction in selenium intake in UK subjects? *Proceedings of the Nutrition Society*, 63: p. 513-517.
69. [Jolliffe JA](#), [Rees K](#), [Taylor RS](#), [Thompson D](#), [Oldridge N](#), [Ebrahim S](#) (2000) Exercise-based rehabilitation for coronary heart disease [Jolliffe JA](#), [Rees K](#), [Taylor RS](#), [Thompson D](#), [Oldridge N](#), [Ebrahim S](#). [Cochrane Database Syst Rev.](#);(4):CD001800.
70. Joseph A, Moysich KB, Freudenheim JL, Shields PG, Bowman ED, Zhang Y, Marshall JR, and Ambrosone CB (2007) Cruciferous Vegetables, Genetic Polymorphisms in Glutathione S-Transferases M1 and T1, and Prostate Cancer Risk Michael A. *NUTRITION AND CANCER*, 50(2), 206–213.
71. Kaaks R and Lukanova A (2002) Effects of weight control and physical activity in cancer prevention: role of endogenous hormone metabolism. *Ann N Y Acad Sci*, 963: p. 268-81.
72. Klein A (2009) SELECT STUDY. *JNCI Journal of the National Cancer Institute* 2009 101(5):283-285.

73. Knekt P , Aromaa A , Maatela J , Alfthan G , Aaran R , Hakama M , Hakulinen T , Peto R , and Teppo L (1990) Serum Selenium and Subsequent Risk of Cancer Among Finnish Men and Women. *J. Natl. Cancer Inst.* 82: 864-868.
74. Knols R, Aaronson NK, Uebelhart D, Fransen J, Aufdemkampe G (2005) Physical exercise in cancer patients during and after medical treatment: A systemic review of randomised and controlled clinical trials. *Journal of Clinical Oncology*, 23(16): p. 3830-3842.
75. Kok FJ, De Bruun AM, Hofman A, et al. (1987) Is serum selenium a risk factor for cancer in men only? *Am J Epidemiol* 125:12-16, 1987.
76. Kortenkamp, A (2008) Breast cancer and exposure to hormonally active chemicals: An appraisal of the scientific evidence. A background briefing paper. ChemTrust, London, April 2008.
77. Kristal AR, [Cohen JH](#), [Qu P](#), [Stanford JL](#). (2002) Associations of energy, fat, calcium and vitamin D with prostate cancer risk. *Cancer Epidemiol Biomarkers Prevent*, 11: p. 719-725.
78. Kroenke CH, et al., Dietary patterns and survival after breast cancer diagnosis. *Journal of Clinical Oncology*, 2005. 23(36): p. 9295-0303.
79. Kroenke CH, et al Weight gain and survival after breast cancer diagnosis. *JCO* 2005. 23(7): p. 1370-1378
80. Kucuk O, [Sarkar FH](#), [Djuric Z](#), [Sakr W](#), [Pollak MN](#), [Khachik F](#), [Banerjee M](#), [Bertram JS](#), [Wood DP Jr](#). (2002) Effects of lycopene supplementation in patients with localized prostate cancer. *Exp Biol Med* (Maywood), 227: p. 881-885.
81. Lahmann PH, Friedenreich C, Schuit AJ, Salvini S, Allen NE, Key TJ, Khaw KT, Bingham S, Peeters PH, Monninkhof E, Bueno-de-Mesquita HB, Wirfält E, Manjer J, Gonzales CA, Ardanaz E, Amiano P, Quirós JR, Navarro C, Martinez C, Berrino F, Palli D, Tumino R, Panico S, Vineis P, Trichopoulou A, Bamia C, Trichopoulos D, Boeing H, Schulz M, Linseisen J, Chang-Claude J, Chapelon FC, Fournier A, Boutron-Ruault MC, Tjønneland A, Føns Johnson N, Overvad K, Kaaks R, Riboli E. (2007) *Cancer Epidemiol Biomarkers Prev.* Jan;16(1):36-42. Epub 2006 Dec 19.
82. Land, C. E. (1995). "Studies of Cancer and Radiation Dose Among Atomic Bomb Survivors: The Example of Breast Cancer." *JAMA* 274(5): 402-407.

83. Leatham A and Velentzis L (2006) DietComplyf: The role of diet, complementary treatment, and lifestyle in breast cancer survival. <http://www.ucl.ac.uk/abc-research-group/Documentations/DietCompLyf%20Protocol%20v6,%20Jan%2006.pdf>.
84. Lee CY (2002) Phytochemicals and apples. *The Lancet*. 359(12): p. 9301.
85. Lee MM, Gomez SL, Chang JS, Wey M (2003) Soy and Isoflavone Consumption in Relation to Prostate Cancer Risk in China. *Cancer Epidemiology, Biomarkers & Prevention* July 1, 2003 12, 665.
86. Li C, Daling J, Porter P, Tang M, Malone K 2009. Relationship between potentially modifiable lifestyle factors and risk of secondary contralateral breast cancer *Journal of Clinical Oncology* vol. 27, No.32, pp4312-5302
87. Lucia A, Earnest C, Perez M. (2003) Cancer-related fatigue: can exercise physiology assist oncologists? *Lancet Oncol*; 4:616-625.
88. Ma J, [Giovannucci E](#), [Pollak M](#), [Leavitt A](#), [Tao Y](#), [Gaziano JM](#), [Stampfer MJ](#). (2004) A prospective study of plasma C-peptide and colorectal cancer risk in men. *J Natl Cancer Inst*, 96: p. 546-53.
89. Ma J, [Pollak MN](#), [Giovannucci E](#), [Chan JM](#), [Tao Y](#), [Hennekens CH](#), [Stampfer MJ](#). (1999) Prospective study of colorectal cancer risk in men and plasma levels of insulin-like growth factor (IGF)-I and IGFbinding protein-3. *J Natl Cancer Inst*, 91: p. 620-5.
90. Madaan S, Abel PD, Chaudhary KS, Hewitt R, Stott MA, Stamp GWH and Lalani EN (2000) Cytoplasmic induction and over-expression of cyclooxygenase-2 in human prostate cancer: implications for prevention and treatment. *International Journal of Urology*, 86: p. 736-741.
91. Mahmud S, Franco E, and [Aprikian A](#). (2003) Prostate cancer and use of nonsteroidal anti-inflammatory drugs: systematic review and meta-analysis. *British Journal of Cancer*. 90: p. 93-99.
92. Marklund SL, [Westman NG](#), [Lundgren E](#), [Roos G](#). (1982) Copper- and zinc-containing superoxide dismutase, manganese-containing superoxide dismutase, catalase, and glutathione peroxidase in normal and neoplastic human cell lines and normal human tissues. *Cancer Research*, 42(5): p. 1955-61.
93. Mehta RG and Moon RC (1991) Characterization of effective chemopreventive agents in mammary gland in vitro using an initiation-promotion protocol. *Anticancer Research*, 11: p. 593-596.

94. McLarty, Jerry, Bigelow, Rebecca L.H., Smith, Mylinh, Elmajian, Don, Ankem, Murali, Cardelli, James A. (2009) Tea Polyphenols Decrease Serum Levels of Prostate-Specific Antigen, Hepatocyte Growth Factor, and Vascular Endothelial Growth Factor in Prostate Cancer Patients and Inhibit Production of Hepatocyte Growth Factor and Vascular Endothelial Growth Factor In vitro. *Cancer Prev Res: 1940-6207.CAPR-08-0167*.
95. McTiernan A, [Ulrich C](#), [Slate S](#), [Potter J](#). (1998) Physical activity and cancer etiology: associations and mechanisms. *Cancer Causes Control*, 9: p. 487-509.
96. Meyerhardt JA, Heseltine D, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Schilsky RL and Fuchs CS (2005) The impact of physical activity on patients with stage III colon cancer: Findings from Intergroup trial CALGB 89803. *Proc Am Soc Clin Oncol*, 24: p. abstract 3534.
97. Minton O, Stone P (2009). A systemic review of the scales used for the measurement of cancer-related fatigue. *Annals of Oncology*, 20, 17-25.
98. Mock V, Burke MB, Sheehan P et al. (1994) A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncol.Nurs.Forum*;21:899-907.
99. Mock V, Pickett M, Ropka ME et al. (2001) Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Pract.* 9:119-127.
100. Mock V, Frangakis C, Davidson NE et al.(2005) Exercise manages fatigue during breast cancer treatment: a randomized controlled trial. *Psychooncology*;14:464-477.
101. Monga U, Garber SL, Thornby J et al. (2007) Exercise prevents fatigue and improves quality of life in prostate cancer patients undergoing radiotherapy. *Arch.Phys.Med.Rehabil*;88:1416-1422.
102. Mutrie N, Campbell AM, Whyte F et al. (2007) Benefits of supervised group exercise programme for women being treated for early stage breast cancer: pragmatic randomised controlled trial. *BMJ*;334:517.
103. National Comprehensive Cancer Network (2009) NCCN Clinical Practice Guidelines in Oncology. Cancer-related fatigue, version 1. 2009.
104. Nomura AM, et al. (2003) Serum insulin-like growth factor I and subsequent risk of colorectal cancer among Japanese-American men. *Am J Epidemiol*, 158: p. 424-31.
105. Ng, K., J. A. Meyerhardt, et al. (2008). "Circulating 25-Hydroxyvitamin D Levels and Survival in Patients With Colorectal Cancer." *J Clin Oncol* 26(18): 2984-2991.

106. Nguyen, T. and D. Ho (2002). "Nonmelanoma skin cancer." *Current Treatment Options in Oncology* 3(3): 193-203.
107. Oldridge NB, Guyatt GH, Fischer ME, and Rimm AA (1988) Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. *JAMA* vol.2 60, 7.
108. Omenn GS, et al., (1996) Risk factors for lung cancer and for intervention effects in CARET, the beta-carotene in retinol efficacy trial. *Journal of the National Cancer Institute*, 88: p. 1550-1559.
109. Onland-Moret, N. C., P. H. M. Peeters, et al. (2005). "Alcohol and Endogenous Sex Steroid Levels in Postmenopausal Women: A Cross-Sectional Study." *J Clin Endocrinol Metab* 90(3): 1414-1419.
110. Ornish D, et al. (2005) Intensive lifestyle changes may affect the progression of prostate cancer. *The Journal of Urology*, 174: p. 1065-1070.
111. Ostroff JS, Jacobsen PB, Moadel AB, Spiro RH, Shah JP, Strong EW, et al. (1995) Prevalence and predictors of continued tobacco use after treatment of patients with head and neck cancer. [Cancer; Jan 15;75\(2\):569-76.](#)
112. Palmqvist R, et al., (2002) Plasma insulin-like growth factor 1, insulin-like growth factor binding protein 3, and risk of colorectal cancer: a prospective study in northern Sweden. *Gut*, 50: p. 642-6.
113. Pantuck AJ, et al. (2006) Phase 11 study of pomegranate juice for men with rising PSA following surgery or RXT for prostate cancer. *Clin Cancer Res*, 12(13): p. 4018-4026.
114. Payne JK, Held J, Thorpe J, Shaw H. (2008) Effect of exercise on biomarkers, fatigue, sleep disturbances, and depressive symptoms in older women with breast cancer receiving hormonal therapy. *Oncol.Nurs.Forum*; 35:635-642.
115. Peehl DM, et al. (1994) Antiproliferative effects of 1, 25-dihydroxyvitamin D3 on primary cultures of human prostatic cells. *Cancer Research*, 54: p. 805-810.
116. Pierce, J. P., L. Natarajan, et al. (2007). "Influence of a Diet Very High in Vegetables, Fruit, and Fiber and Low in Fat on Prognosis Following Treatment for Breast Cancer: The Women's Healthy Eating and Living (WHEL) Randomized Trial." *JAMA* 298(3): 289-298.

117. Quadrilatero J and Hoffman-Goetz L, (2003) Physical activity and colon cancer. Asystematic review of potential mechanisms. J Sports Med Phys Fitness, 43: p. 121-138.
118. Reeves G, Pirie K, Beral V et al (2007) Cancer incidence and mortality in relation to BMI in the Million Women Study. BMJ, 335, 1134.
119. Richardson, G. E., M. A. Tucker, et al. (1993). "Smoking Cessation after Successful Treatment of Small-Cell Lung Cancer Is Associated with Fewer Smoking-related Second Primary Cancers." Annals of Internal Medicine 119(5): 383-390.
120. Rier SE, Martin DC, Bowman RE, Dmowski WP, Becker JL (1993), Endometriosis in rhesus monkeys (*Macaca mulatta*) following chronic exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Fundam Appl Toxicol 21:433-441 (1993).
121. Rodriguez C et al, (2004) Vitamin E supplements and the risk of prostate cancer. Cancer Epidemiol Biomarkers Prevent, 13: p. 378-382.
122. Rogers L, Hopskin-Price, Vicari et al. (2009) Physical Activity and Health Outcomes Three Months After Completing a Physical Activity Behavior Change Intervention: Persistent and Delayed Effects. Cancer Epidemiol Biomarkers Prev, 18(5):1410-8.
123. Rohan TE, Hiller JE, and McMichael AJ. (1993) Dietary factors and survival from breast cancer. Nutr Cancer, 1993. 20: p. 167-77.
124. Rose DP (1992) Dietary fibre, phytoestrogens and breast cancer. Nutrition, 8: p. 47-51.
125. Sandler RS, et al. (2003) A randomised trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. The New England Journal of Medicine, 348(10): p. 883-890.
126. Schmitz K, Ahmed R, Troxel A, A Cheville A, Smith R, LLewis-Grant, Bryan C, Q. Greene 2009 Weight lifting programmes for women post axillary node clearance reduces lymphoedema related events. New England Journal of Medicine Vol 361: 664-673 no.7.
127. Schoonen WM, et al. (2005) Alcohol consumption and the risk of prostate cancer in middle-aged men. Int J Cancer, 113: p. 133-140.
128. Schreinemachers DM and [Everson RB](#). (1994) Aspirin use and lung, colon and breast cancer incidence in a prospective study. Epidemiology, 5: p. 138-146.

129. Schwartz GG et al. (1994) Human prostate cancer cells: Inhibition of proliferation by vitamin D analogs. *Anticancer Research*, 1994. 14: p. 1077-1081.
130. Schwartz, L. H., M. Ozsahin, et al. (1994). "Synchronous and metachronous head and neck carcinomas." *Cancer* 74(7): 1933-1938.
131. Schwarz S, Obermu UC, Iler-Jevic, Hellmis E, Koch W, Jacobi G, and Biesalski HK (2008) Lycopene Inhibits Disease Progression in Patients with Benign Prostate Hyperplasia. *Journal of nutrition and disease J. Nutr.* 138: 49–53, 2008.
132. Scripture CD and Figg WD (2006) Drug interactions in cancer therapy. *Nature Reviews Cancer* 6, 546–558 (1 July 2006).
133. Segal RJ, Reid RD, Courneya KS et al.(2003) Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *J.Clin.Oncol.*;21:1653-1659.
134. Segal RJ, Reid RD, Courneya KS et al.(2009) Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. *J Clin Oncol.*;20;27:344-351.
135. Segar M, et al. (1998) The affect of aerobic exercise on self-esteem and depressive and anxiety symptoms among breast cancer survivors. *Oncol Nurs Forum*, 25: p. 107-113.
136. Smedby KE, Hjalgrim H, Melbye M, Torrång A, Rostgaard K, Munksgaard L, et al.(2005) Ultraviolet radiation exposure and risk of malignant lymphomas. *J Natl Cancer Inst*;97:199–209.
137. Soliman, S., W. J. Aronson, et al. (2009). "Analyzing Serum-Stimulated Prostate Cancer Cell Lines After Low-Fat, High-Fiber Diet and Exercise Intervention." *eCAM*: nep031.
138. Sonn GA, Aronson W, and Litwin MS (2005) Impact of diet on prostate cancer: A review. *Prostate cancer and prostate disease*, 8: p. 304-310.
139. Spentzos D, Mantzoros C, Regan MM, Morrissey ME (2003) *Clinical Cancer Research* August 2003 9, 3282.
140. Sprod LK (2009) Considerations for Training Cancer Survivors Strength and conditioning journal volume 31, number 1. Rocky Mountain Cancer Rehabilitation Institute, University of Northern Colorado, Greeley, Colorado.

141. Stivala LA, et al. (2000) The antiproliferative effect of beta-carotene requires p21waf1/cip1 in normal human fibroblasts. *Journal of Biochemistry*, 267: p. 2290-2296.
142. Suikkari AM, et al. (1988) Insulin regulates the serum levels of low molecular weight insulin-like growth factor-binding protein. *J Clin Endocrinol Metab*, 66: p. 266-72.
143. Svilaas A, et al. (2004) Intake of antioxidants in coffee, wine and vegetables are correlated with plasma carotenoids in humans. *Journal of Nutrition*, 134: p. 562-567.
144. Terry P, et al. (2001) Fatty fish consumption and risk of prostate cancer. *Lancet*, 357: p. 1764-1766.
145. Terry PD, Rohan TE, and Wolk A (2003) Intakes of fish and marine fatty acids and the risks of cancers of the breast and prostate and of other hormone-related cancers: A review of the epidemiologic evidence. *American Journal of Clinical Nutrition*, 77: p. 532-543.
146. Thomas R, Daly M, and Perryman J (2000) Forewarned is forearmed - Randomised evaluation of a preparatory information film for cancer patients. *European Journal of Cancer*, 36(2): p. 52-53.
147. Thomas R, et al. (2005) Dietary advice combined with a salicylate, mineral and vitamin supplement (CV247) has some tumour static properties - a phase II study. *Nutrition and science*, 2005. 35(6): p. 436-451.
148. Thomas R et al. (2006) Diet, salicylates and Prostate cancer. *British Journal of Cancer Management*,.
149. Thomas R and Davies N (2007) Cancer – the roles of exercise in prevention and progression. *Nutrition and Food Science*, Volume 37; Issue 5.
150. Thomas R and Davies N (2007) Lifestyle during and after cancer Treatments. *Clinical Oncology*, 19, pp 616-627.
151. Thomas R, Blades M, Williams M (2007) Can dietary intervention alter prostate cancer progression. *Nutrition & Food Science*, 2007 vol 37, no.1 pp 24-36.
152. Thomas R (2008) Lifestyle after cancer – the facts. Health Education Publications (www.cancernet.co.uk/books.htm)

153. Thomas R, Williams M, and Davies N (2009) Should oncology units establish Lifestyle Clinics? *Clinical Focus on Cancer Medicine*, (1) 2; 38-48.
154. Thomas R, Taylor T, Williams M (2009) Development of a lifestyle exit tool box abstract and poster. *ECCO, EJC* vol 7, no.2, p.210; sup.3608.
155. Thomas R, Williams M, and Taylor T (2009) Life after cancer – rehabilitation at home can improve well-being and survival. *British Journal of Home Healthcare*, 5(1):10-12.
156. Thomas R (2009) Exercise after Cancer – How to do it? *ICAN Journal*; September 2009.
157. Thun, M. J., R. Peto, et al. (1997). "Alcohol Consumption and Mortality among Middle-Aged and Elderly U.S. Adults." *N Engl J Med* **337**(24): 1705-1714.
158. van der Bol JM, Mathijssen RHJ, Loos WJ, Friberg LE, van Schaik RHN, de Jonge MJA, Planting AS, Verweij J, Sparreboom A, de Jong FA. (2007) Cigarette Smoking and Irinotecan Treatment: Pharmacokinetic Interaction and Effects on Neutropenia. *Journal of Clinical Oncology*, Vol 25, No 19 (July 1), pp. 2719-2726.
159. Velthuis MJ, Agasi-Idenburg SC, Aufdemkampe G, Wittink HM (in press) The effect of physical exercise on cancer-related fatigue during cancer treatment: a meta-analysis of Randomised Controlled Trials *Clinical Oncology*, 2009 (in print).
160. Wagner LI, Cella D. (2004) Fatigue and cancer: causes, prevalence and treatment approaches. *Br.J.Cancer*;91:822-828.
161. Warren RS, et al. (1996) Induction of vascular endothelial growth factor by insulin-like growth factor 1 in colorectal carcinoma. *J Biol Chem*, 271: p. 29483-8.
162. Westerlind KC (2003) Physical activity and cancer prevention-mechanisms. *Med Sci Sports Exerc.*, 2003. 35: p. 1834-40.
163. Wilkinson S and Chodak GW, (2003) Critical review of complementary therapies for prostate cancer. *Journal of Clinical Oncology*, 21(11): p. 2199-2210.
164. Windsor PM, Nicol KF, Potter J. (2004) A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. *Cancer*;101:550-557.
165. Wu A, Pike M, and Stram D (1999) Dietary fat intake, serum estrogen levels, and the risk of breast cancer. *J Natl Cancer Inst*, 91: p. 529-534.

166. Yu GP et al. (1997) The effect of smoking after treatment for Cancer. *Cancer Detect Prev* 21:487-509.
167. Yu H and Rohan T (2000) Role of the insulin-like growth factor family in cancer development and progression. *J Natl Cancer Inst*; 92: p. 1472-89.
168. Zhao XY, et al. (1999) Induction of androgen receptor by 1 alpha, 25-dihydroxyvitaminD3 and 9-cis retinoic acid in LNCaP human prostate cancer cells. *Endocrinology*, 140: p. 1205-1212.