Life Style Prevention of Cancer Recurrence: The Yin and the Yang

Franco Berrino

Abstract

There is increasing evidence that lifestyle after the diagnosis of cancer may affect prognosis. Several studies have shown that a Western dietary pattern, obesity, weight gain, a sedentary lifestyle, metabolic syndrome, high serum levels of insulin, growth factors, and inflammatory cytokines after the diagnosis of cancer are associated with an increased incidence of recurrences. Most studies have been on breast and colon cancer. However, in the clinical management of cancer, little attention is presently paid to improving lifestyle and controlling body weight. Lifestyle intervention trials are needed to corroborate or confute the observational results on cancer recurrences, but, even now, there is no contraindication to promoting moderate physical exercise, moderate calorie restriction (CR), and a Mediterranean dietary pattern. In fact, the AICR/WCRF 2007 systematic literature review recommends cancer patients to adopt the lifestyle recommended for the prevention of cancer. Interestingly, the evidence-based AICR/WCRF recommendations coincide with traditional rules, based on far Eastern philosophy, of avoiding extremely *yin* food, such as sugared beverages and calorie-dense foods, and extremely *yang* food, such as processed meat, and relying on the equilibrium of slightly *yang* food, such as whole-grain unprocessed cereals, eaten with slightly *yin* food, such as legumes and vegetables.

Keywords

Macrobiotic diet · Lifestyle · Mediterranean dietary pattern · Breast cancer

F. Berrino (✉)
Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian, 1, 20133, Milan, Italy
e-mail: franco.berrino@istitutotumori.mi.it

V. Zappia et al. (eds.), *Advances in Nutrition and Cancer*,
Cancer Treatment and Research 159, DOI: 10.1007/978-3-642-38007-5_20,

Abbreviations

CMF Cyclophosphamide/methotrexate/5-fluorouracil
CR Calorie restriction
MS Metabolic syndrome

Contents

1 Introduction

Worldwide, we are entering a period of unprecedented high prevalence of age-related chronic non-communicable diseases, whose related disabilities are projected to inflate into an unprecedented economic and social challenge. Human chronic diseases are complex non-linear processes that depend on a large number of interconnected genetic and metabolic pathways which should be tackled with a many faceted preventive strategy. In animals, calorie restriction (CR) is the most potent dietary intervention for preventing cancer and other age-related chronic diseases, and for prolonging life. In humans, calorie-dense diet and sedentary lifestyle are responsible for the growing prevalence of metabolic syndrome (MS), which, together with tobacco, is the major preventable cause of the most prevalent chronic diseases, mediated by the increased availability of insulin, growth factors, and inflammatory cytokines. There is increasing evidence that MS is also a major determinant of cancer recurrence [6, 44, 46, 49, 55, 59, 60]. We and others have shown that a sustainable CR, associated with decreased prevalence of MS, can be obtained through a comprehensive change in dietary habits, reducing animal food and refined carbohydrates, and increasing whole-grain cereal products, legumes, and vegetables [2, 13]. Chronic diseases are largely due to modifiable Western lifestyle factors. To date, however, investment in promoting potentially preventive and sustainable lifestyle modification is disproportionately low relative to its potential return.

Progress in cancer and other chronic disease biology has been extremely fast in the last few decades, emphasizing the relevance of complexity as opposed to the previously dominant reductionist view of nature, which has been very productive

for the prevention of cardiovascular diseases (based on treatment of specific risk factors) but largely ineffective for cancer. The cancer chemoprevention experiments carried out so far in humans do not seem to have paid much attention to this evolving view of complexity. Most were based on the supplementation or the avoidance of a single or a few nutrients, and most failed or ended with dubious results. Multi-faceted intervention is probably needed to favourably affect the complex biological systems involved in the development of cancer. A single agent or factor acting on a single or a few pathways might actually fail because of the existence of redundant vicarious pathways, or even be dangerous because of its interference with potentially preventive pathways.

2 The "Yin" Food and the "Yang" Food

All foods derive from living organisms, either animal or plant, which are extremely complex and have evolved, together with human ancestors, over millions of years. The availability of food has influenced human evolution, and vice versa. Poisonous foods have been progressively recognized and eliminated from the diet, and natural selection has favoured the adoption of food patterns permitting healthy reproductive life. In the last 10–30,000 years, cereals have become the staple food of almost all human populations, and humans had experienced the advantage of mixing cereals and legumes in the same dish thousands of years before acquiring the knowledge of their complementary aminoacidic composition. Two recent large cohort studies on the intake of dietary fibres and mortality, the EPIC study in Europe [8] and the NCI-ARP study in the US [45], consistently showed that a high intake of cereal fibres is associated with lower mortality from cancer, cardiovascular, pulmonary, gastrointestinal, and infectious diseases. In addition, vegetable fibres were associated with some protection, but not fruit fibres. Interestingly, the isolated administration of whole-grain cereal components—fibres, vitamins, or minerals—did not seem to elicit any protective effect [26], suggesting more than an additive influence of cereal constituents on health, the so-called "food synergy" [23–25].

Whole-grain cereals (mainly brown rice, millet, barley, oats) and occasionally buckwheat and wheat pasta are the basic components of a macrobiotic diet, which also includes 20–30 % locally grown vegetables, 5–10 % beans, including traditional soy products, sea vegetables and occasionally fruits, nuts, and fish [33]. Interestingly enough, the 2007 WCRF/AICR recommendations for the prevention of cancer[1] (Table 1) broadly coincide with the macrobiotic recommendations of avoiding the habitual intake of extremely "yin" food, such as sugar and sugared beverages, alcoholic beverages, and refined flours, as well as of extremely "yang" food, such as processed meat, salty food, and red meat, while the central recommendation is to "Eat mostly food of plant origin, with a variety of non-starchy

[1] www.dietandcancerreport.org

Table 1 WCRF recommendations

• Be as lean as possible within the normal range of body weight
• Be physically active as part of everyday life
• Limit consumption of energy-dense food and avoid sugary drinks
• Eat mostly food of plant origin, with "a variety of non-starchy vegetables and of fruit every day" and "relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal"
• Limit intake of red meat and avoid processed meat
• Limit alcoholic drinks
• Limit consumption of salt and avoid mouldy cereals or pulses
• Aim to meet nutritional needs through diet alone
• Mothers to breastfeed; children to be breastfed
• Cancer survivors to follow the recommendations for cancer prevention

Fig. 1 Tao pictogram representing the concept of yin and yang

vegetables and of fruit every day and with unprocessed cereals and/or pulses with every meal", which is also the basic characteristic of the Mediterranean diet, as well as the staple food of most populations before the industrial revolution: pasta with beans in Italy, cuscus with chickpeas in north Africa, rice with soy products in Asia, maize with black beans in central America, and millet with peanuts in Black Africa.

Table 2 Nutritional WCRF recommendations ordered by yin–yang criteria

Avoid sugary drinks	▼▼▼
Limit alcoholic drinks	▼▼
Limit energy-dense food	▼
Eat mostly food of plant origin with relatively unprocessed cereals, pulses, and vegetables	
Limit intake of red meat	▲
Limit consumption of salt	▲▲
Avoid processed meat	▲▲▲

In Chinese philosophy, the concept of *yin–yang* is used to describe how polar opposites or seemingly contrary forces are interconnected and interdependent in the natural world, and how they cause everything to happen. Yin and yang are not opposing forces, but complementary forces. Everything has both yin and yang aspects. The concept of yin and yang is present in the Tao pictogram (Fig. 1), symbolically representing a walking man sustaining on his shoulder a bamboo cane with two baskets, one carrying the yin energy and the other the yang energy. Only if there is a perfect equilibrium between the two energies can the man make his way towards the Tao. Classically, "yang" refers to the "sunny side", and "yin" to the "shadowy side". While "yin" is dark, passive, feminine, cold, wet, diffuse, weak and is associated with the earth and the night, "yang" is bright, active, masculine, hot, dry, focused, strong and associated with the sky and the sun. Animal food is yang, especially red and salted meat, and vegetable food is yin, the most yin being refined foods such as oils, alcoholic beverages, and sugar.

Table 2 shows the WCRF/AICR recommendations ordered according to the macrobiotic classification of food in terms of yin and yang. Yang is symbolized by a triangle soundly resting on its base, while yin is symbolized by a triangle in difficult equilibrium on its vertex. In synthesis, the WCRF/AICR recommendations are to avoid extremely yin and yang food, to limit unbalanced yin and yang food, and to rest on slightly yang food, such as whole-grain unprocessed cereals, equilibrated by slightly yin food, such as legumes and vegetables.

In fact, observing the gastronomic traditions of all populations living in temperate climates, one usually notices attempts to equilibrate yang and yin food: fish is usually served with a boiled potato, turkey is filled with chestnuts, red meat is served with some salad and a glass of wine; in Italy, salted ham is served with melon; in Sicily, citrus fruits are eaten with salt; and hamburger, very yang because made of red meat and cooked at a high temperature, is usually eaten with very yin sugared beverages on ice. Only in very cold (yin) climates, one may have two very yang food at breakfast, such as egg and bacon. In hot climates one would prefer yin fruits and sweets. A key principle of the Taoist philosophy is to emphasize *wu-wei* (literally non-action), action through non-action, basically meaning respecting nature, harmonizing with nature, "naturalness", and, in nutrition, choosing natural, simple, harmonizing foods, instead of extremely processed foods.

3 Synergy in Food

The advantage of choosing simple food profiting from the synergy between different food components is increasingly recognized [25]. The bioavailability of omega-3 fatty acids is several folds higher if they are taken from fish rather than from supplements. Supplementing a liposoluble vitamin may decrease the absorption of other vitamins that use the same transporter mechanism. The results of most randomized controlled trials of nutrient supplements (mainly antioxidant vitamins and minerals and B vitamins) to prevent cancer or cardiovascular diseases

were either null or showed adverse effects. On the contrary, observational studies on food patterns showed a lower incidence of chronic disease, in persons characterized by a high score of prudent or Mediterranean food pattern. A significantly lower risk was reported for diabetes [51], cardiovascular diseases [18, 30], stroke [1], Alzheimer [53], and several cancers, including breast [9, 57, 61], stomach [3], colon [15], and pancreatic cancer [27].

Constituents of natural foods are coordinated, and their concentration varies in different environments. Vegetables growing in the mountains, for instance, are richer in polyunsaturated fatty acids, which protect from low temperatures, and foods containing high quantities of polyunsaturated fatty acids are usually richer in antioxidant phytochemicals. There is increasing evidence that phytochemicals affect gene expression, favouring or inhibiting DNA methylation, histone acetylation, or micro-RNA. Specific DNA methylations and histone modifications, usually associated with pro-inflammatory micro-environments, have been implicated in several cancers. In principle, as epigenetic changes can be transmitted over consecutive mitotic divisions, those occurring before conception or during embryonic development will have a much greater impact on the overall epigenetic status of the organism. Nevertheless, at any age, environmental factors, such as diet and physical activity, may modify DNA methylation and histone acetylation [14, 36]. Global hypomethylation and site-specific hypermethylation are common features of human tumours. Diet can profoundly alter epigenetic patterns, but the causal link between diet and epigenetics in the development of human disease is still poorly understood. A challenging research field is developing to determine which adverse epigenomic marks are reversible by specific drugs, nutrients, or lifestyle changes. Over 50 bioactive phytochemicals have been demonstrated to be active on DNA methyltransferase, or histone acetylase/deacetylase. Experimental studies on animals or cultured human cell lines support their role in the prevention of cancer, but have often been conducted at concentrations far beyond those documented in humans. It is very difficult to predict from these results the effects of these substances on disease prevention in humans. There is evidence, however, that continuous exposure at physiological concentrations can remodel the epigenome in a cumulative fashion [52]. Moreover, in these experiments, whole food extracts usually have significantly greater physiological effects than isolated specific constituents: “Mother Nature knew what she was doing when she created plant foods: vegetables, fruit, whole grains, nuts, and legumes are great examples of foods that are rich in a combination of important vitamins, minerals, fiber, protein, antioxidants, and more” (cited from [24]). As there is still much we do not know or do not understand about the interaction of biologically active plant food components, it is better to eat food as close to its natural form as possible: let us harmonize with nature.

4 Cancer and Lifestyle

Several studies have shown that a Western dietary pattern, obesity, weight gain, a sedentary lifestyle, metabolic syndrome, high serum levels of insulin, and growth factors after the diagnosis of cancer are associated with an increased incidence of recurrences and with lower cancer-specific survival. Most studies were on breast and colon cancer. However, in the clinical management of cancer, little attention is presently paid to improving lifestyle and controlling body weight.

Lifestyle intervention trials are needed to corroborate or confute the observational results on cancer recurrences, but, even now, there is no contraindication to promoting moderate physical exercise, moderate CR, and a Mediterranean dietary pattern. Several studies showed that obese people have lower overall and disease-free survival when diagnosed with breast cancer [10, 37, 50, 54], colorectal cancer [11, 20], and prostate cancer [17, 38], independently from the stage at diagnosis and other biological characteristics of the disease. Recently, a clinical study suggested that obesity is an unfavourable prognostic factor also for non-Hodgkin lymphoma [16]. A meta-analysis of 43 studies that followed up breast cancer patients showed poorer survival among obese compared with non-obese women, for both overall [HR 1.33; 95 % confidence interval (CI) 1.21, 1.47] and breast cancer–specific survival (HR 1.33; 95 % CI 1.19, 1.50). Similar results were obtained using waist–hip ratio as the measure of obesity (HR 1.31; 1.08, 1.58). The effect was present in both premenopausal and postmenopausal patients, and in treatment and observational cohorts [50].

There is evidence, moreover, that weight gain after the diagnosis of breast cancer is associated with an increased risk of total and breast cancer mortality. In a study [43], each 5-kg gain was associated with a 13 % increase in breast cancer–specific mortality; weight loss after diagnosis was associated with increased mortality from all causes, and mortality from breast cancer was (non-significantly) lower if compared to stable weight. Several studies also reported that the weight gain usually observed during CMF-based adjuvant chemotherapy was associated with a worse prognosis [5, 31]. We showed that weight gain during adjuvant chemotherapy can be prevented [59]. Little attention, however, is presently paid to weight control in the clinical management of breast cancer.

A randomized controlled trial carried out on 2,500 breast cancer patients to test the efficacy of reducing dietary fat intake showed a borderline significant 24 % reduction in new breast cancer events (local and distance recurrences and contralateral breast cancer) [7]. In this study, women in the intervention arm lost, on average, 2.1 kg over 5-year follow-up. Another trial carried out on over 3,000 patients to test the effect of reducing fat intake and increasing the consumption of fruit and vegetables (mainly through fruit and vegetable juices) did not find any protection; in this case, however, the design was isocaloric, and the women randomized in the intervention group actually gained some weight [48]. The likely reason for such a discrepancy is that a moderate calorie restriction may protect from breast cancer recurrence.

Observational studies on thousands of patients operated for breast cancer [21, 22, 47] or colorectal cancer [20, 40] showed that those who practise moderate physical exercise after diagnosis experience a lower risk of recurrence and death. In colon cancer patients, there is no evidence of any effect in stage I or stage IV, but there is a marked effect in stage II and III. In breast cancer patients, the effect of physical activity is apparently confined to oestrogen receptor–positive tumours, with a reduction in cancer-specific mortality of the order of 30–50 % for women practising at least 30 min per day of a physical exercise whose intensity corresponds to brisk walking. The mechanism by which physical exercise is protective is likely to involve its effect on insulin sensitivity.

An observational study of the dietary pattern of colon cancer patients participating in a randomized study of adjuvant chemotherapy showed that a high score in Western diet was associated with a significantly increased risk of recurrences. Foods with higher factor load included cheese, fat condiments, margarines, sweets, red meat, and processed meat [39]. Similar studies on breast cancer patients, on the contrary, found that a Western dietary pattern was associated with lower all-cause mortality but not breast cancer–specific mortality [32, 35]. A diet rich in dairy products and poor in vegetables has also been found to be associated with worse survival in two studies on ovarian cancer patients [12, 41]. These studies, however, relied only on the cases' recall of prediagnosis dietary intake. Observational studies suggest that specific vegetable food, such as soy food [4, 19, 29, 56] and cruciferous vegetables, may help to prevent breast cancer recurrences, both in patients under hormonal treatment and not. Also marine fatty acids from food are likely to be associated with a reduced risk of breast cancer recurrence (and all-cause mortality): a study that assessed dietary intake with repeated 24-h recalls over 6 years found that breast cancer patients whose consumption of long-chain omega-3 fatty acids was in the upper two tertiles had 25 % reduced risk of additional breast cancer events [27, 58]. The consumption of omega-3 supplements did not show any protective effect. Studies on multivitamin use and breast cancer outcome have given intriguing and contradictory results [34, 42].

The DIANA (DIet and ANdrogen) trials of dietary intervention for the prevention of breast cancer showed that a few months of Mediterranean and macrobiotic diet are sufficient to favourably modify the metabolic and endocrine characteristics of women at high risk of breast cancer, namely to reduce insulin and the bioavailability of growth factors and sex hormones [2, 28]. The ongoing DIANA-5 project [60] is a randomized controlled trial of diet and physical activity on 2,000 breast cancer patients at high risk of recurrence because of MS and/or high serum insulin or testosterone level. Its aim is to test the hypothesis that it would be possible to significantly reduce breast cancer recurrences through a comprehensive lifestyle modification, which includes moderate physical exercise, moderate calorie restriction, and a diet mostly based on food of plant origin, with an ample variety of unrefined grains, legumes, and seasonal vegetables and fruit, according to the 2007 World Cancer Research Fund recommendations.[2]

[2] www.dietandcancerreport.org

If this and other studies fulfil the promise of reducing cancer-related morbidity and improving quality of life, dietary advice and weight control support for breast cancer survivors shall become a new standard of care.

References

1. Agnoli C, Krogh V, Grioni S, Sieri S et al (2011) A priori-defined dietary patterns are associated with reduced risk of stroke in a large Italian cohort. J Nutr 141:1552–1558
2. Berrino F, Bellati C, Secreto G et al (2001) Reducing bioavailable sex hormones through a comprehensive change in diet: the diet and androgens (DIANA) randomized trial. Cancer Epidemiol Biomarkers Prev 10:25–33
3. Buckland G, Agudo A, Lujan L et al (2010) Adherence to a Mediterranean diet and risk of gastric adenocarcinoma within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study. Am J Clin Nutr 91:381–390
4. Caan BJ, Natarajan L, Parker B et al (2011) Soy food consumption and breast cancer prognosis. Cancer Epidemiol Biomarkers Prev 20:854–858
5. Camoriano JK, Loprinzi CL, Ingle JN et al (1990) Weight change in women treated with adjuvant therapy or observed following mastectomy for node-positive breast cancer. J Clin Oncol 8:1327–1334
6. Castillejos-Molina R, Rodriguez-Covarrubias F et al (2011) Impact of metabolic syndrome on biochemical recurrence of prostate cancer after radical prostatectomy. Urol Int 87:270–275
7. Chlebowski RT, Blackburn GL, Thomson CA et al (2006) Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. J Natl Cancer Inst 98:1767–1776
8. Chuang SC, Norat T, Murphy N et al (2012) Fiber intake and total and cause-specific mortality in the European Prospective Investigation into Cancer and Nutrition cohort. Am J Clin Nutr 96:164–174
9. Cottet V, Touvier M, Fournier A et al (2009) Postmenopausal breast cancer risk and dietary patterns in the E3N-EPIC prospective cohort study. Am J Epidemiol 170:1257–1267
10. Dawood S, Broglio K, Gonzalez-Angulo AM et al (2008) Prognostic value of body mass index in locally advanced breast cancer. Clin Cancer Res 14:1718–1725
11. Dignam JJ, Polite BN, Yothers G et al (2006) Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. J Natl Cancer Inst 98:1647–1654
12. Dolecek TA, McCarthy BJ, Joslin CE et al (2010) Prediagnosis food patterns are associated with length of survival from epithelial ovarian cancer. J Am Diet Assoc 110:369–382
13. Esposito K, Marfella R, Ciotola M et al (2004) Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA 292:1440–1446
14. Fraga MF, Ballestar E, Paz MF et al (2005) Epigenetic differences arise during the lifetime of monozygotic twins. Proc Natl Acad Sci USA 102:10604–10609
15. Fung TT, Hu FB, Wu K et al (2010) The Mediterranean and dietary approaches to stop hypertension (DASH) diets and colorectal cancer. Am J Clin Nutr 92:1429–1435
16. Geyer SM, Morton LM, Habermann TM et al (2010) Smoking, alcohol use, obesity, and overall survival from non-Hodgkin lymphoma: a population-based study. Cancer 116:2993–3000
17. Gong Z, Agalliu I, Lin DW et al (2007) Obesity is associated with increased risks of prostate cancer metastasis and death after initial cancer diagnosis in middle-aged men. Cancer 109:1192–1202

18. Guallar-Castillon P, Rodriguez-Artalejo F, Tormo MJ et al (2012) Major dietary patterns and risk of coronary heart disease in middle-aged persons from a Mediterranean country: the EPIC-Spain cohort study. Nutr Metab Cardiovasc Dis 22:192–199
19. Guha N, Kwan ML, Quesenberry CP et al (2009) Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: the Life After Cancer Epidemiology study. Breast Cancer Res Treat 118:395–405
20. Haydon AM, Macinnis RJ, English DR et al (2006) Effect of physical activity and body size on survival after diagnosis with colorectal cancer. Gut 55:62–67
21. Holick CN, Newcomb PA, Trentham-Dietz A et al (2008) Physical activity and survival after diagnosis of invasive breast cancer. Cancer Epidemiol Biomarkers Prev 17:379–386
22. Holmes MD, Chen WY, Feskanich D et al (2005) Physical activity and survival after breast cancer diagnosis. JAMA 293:2479–2486
23. Jacobs DR Jr, Steffen LM (2003) Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. Am J Clin Nutr 78:508S–513S
24. Jacobs DR Jr, Tapsell LC (2007) Food, not nutrients, is the fundamental unit in nutrition. Nutr Rev 65:439–450
25. Jacobs DR Jr, Gross MD, Tapsell LC (2009) Food synergy: an operational concept for understanding nutrition. Am J Clin Nutr 89:1543S–1548S
26. Jacobs DR, Pereira MA, Meyer KA et al (2000) Fiber from whole grains, but not refined grains, is inversely associated with all-cause mortality in older women: the Iowa women's health study. J Am Coll Nutr 19:326S–330S
27. Jiao L, Mitrou PN, Reedy J et al (2009) A combined healthy lifestyle score and risk of pancreatic cancer in a large cohort study. Arch Intern Med 169:764–770
28. Kaaks R, Bellati C, Venturelli E et al (2003) Effects of dietary intervention on IGF-I and IGF-binding proteins, and related alterations in sex steroid metabolism: the diet and androgens (DIANA) randomised trial. Eur J Clin Nutr 57:1079–1088
29. Kang X, Zhang Q, Wang S et al (2010) Effect of soy isoflavones on breast cancer recurrence and death for patients receiving adjuvant endocrine therapy. CMAJ 182:1857–1862
30. Keys AB, Keys M (1975) Eat well and stay well the Mediterranean way. Doubleday, Garden City
31. Kroenke CH, Chen WY, Rosner B et al (2005a) Weight, weight gain, and survival after breast cancer diagnosis. J Clin Oncol 23:1370–1378
32. Kroenke CH, Fung TT, Hu FB et al (2005b) Dietary patterns and survival after breast cancer diagnosis. J Clin Oncol 23:9295–9303
33. Kushi LH, Cunningham JE, Hebert JR et al (2001) The macrobiotic diet in cancer. J Nutr 131:3056S–3064S
34. Kwan ML, Greenlee H, Lee VS et al (2011) Multivitamin use and breast cancer outcomes in women with early-stage breast cancer: the Life After Cancer Epidemiology study. Breast Cancer Res Treat 130:195–205
35. Kwan ML, Weltzien E, Kushi LH et al (2009) Dietary patterns and breast cancer recurrence and survival among women with early-stage breast cancer. J Clin Oncol 27:919–926
36. Ling C, Groop L (2009) Epigenetics: a molecular link between environmental factors and type 2 diabetes. Diabetes 58:2718–2725
37. Loi S, Milne RL, Friedlander ML et al (2005) Obesity and outcomes in premenopausal and postmenopausal breast cancer. Cancer Epidemiol Biomarkers Prev 14:1686–1691
38. Ma J, Li H, Giovannucci E et al (2008) Prediagnostic body-mass index, plasma C-peptide concentration, and prostate cancer-specific mortality in men with prostate cancer: a long-term survival analysis. Lancet Oncol 9:1039–1047
39. Meyerhardt JA, Niedzwiecki D, Hollis D et al (2007) Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. JAMA 298:754–764
40. Meyerhardt JA, Ogino S, Kirkner GJ et al (2009) Interaction of molecular markers and physical activity on mortality in patients with colon cancer. Clin Cancer Res 15:5931–5936

41. Nagle CM, Purdie DM, Webb PM et al (2003) Dietary influences on survival after ovarian cancer. Int J Cancer 106:264–269
42. Nechuta S, Lu W, Chen Z et al (2011) Vitamin supplement use during breast cancer treatment and survival: a prospective cohort study. Cancer Epidemiol Biomarkers Prev 20:262–271
43. Nichols HB, Trentham-Dietz A, Egan KM et al (2009) Body mass index before and after breast cancer diagnosis: associations with all-cause, breast cancer, and cardiovascular disease mortality. Cancer Epidemiol Biomarkers Prev 18:1403–1409
44. Oh SW, Park CY, Lee ES et al (2011) Adipokines, insulin resistance, metabolic syndrome, and breast cancer recurrence: a cohort study. Breast Cancer Res 13:R34
45. Park Y, Subar AF, Hollenbeck A et al (2011) Dietary fiber intake and mortality in the NIH-AARP diet and health study. Arch Intern Med 171:1061–1068
46. Pasanisi P, Berrino F, De Petris M et al (2006) Metabolic syndrome as a prognostic factor for breast cancer recurrences. Int J Cancer 119:236–238
47. Patterson RE, Cadmus LA, Emond JA et al (2010) Physical activity, diet, adiposity and female breast cancer prognosis: a review of the epidemiologic literature. Maturitas 66:5–15
48. Pierce JP, Natarajan L, Caan BJ 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 298:289–298
49. Post JM, Beebe-Dimmer JL et al (2011) The metabolic syndrome and biochemical recurrence following radical prostatectomy. Prostate Cancer 2011:245642
50. Protani M, Coory M, Martin JH (2010) Effect of obesity on survival of women with breast cancer: systematic review and meta-analysis. Breast Cancer Res Treat 123:627–635
51. Romaguera D, Guevara M, Norat T et al (2011) Mediterranean diet and type 2 diabetes risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study: the InterAct project. Diabetes Care 34:1913–1918
52. Scalbert A, Manach C, Morand C et al (2005) Dietary polyphenols and the prevention of diseases. Crit Rev Food Sci Nutr 45:287–306
53. Scarmeas N, Stern Y, Mayeux R et al (2009) Mediterranean diet and mild cognitive impairment. Arch Neurol 66:216–225
54. Sestak I, Distler W, Forbes JF et al (2010) Effect of body mass index on recurrences in tamoxifen and anastrozole treated women: an exploratory analysis from the ATAC trial. J Clin Oncol 28:3411–3415
55. Shen Z, Ye Y, Bin L et al (2010) Metabolic syndrome is an important factor for the evolution of prognosis of colorectal cancer: survival, recurrence, and liver metastasis. Am J Surg 200:59–63
56. Shu XO, Zheng Y, Cai H et al (2009) Soy food intake and breast cancer survival. JAMA 302:2437–2443
57. Sieri S, Krogh V, Pala V et al (2004) Dietary patterns and risk of breast cancer in the ORDET cohort. Cancer Epidemiol Biomarkers Prev 13:567–572
58. Thomson CA, Rock CL, Thompson PA et al (2011) Vegetable intake is associated with reduced breast cancer recurrence in tamoxifen users: a secondary analysis from the women's healthy eating and living study. Breast Cancer Res Treat 125:519–527
59. Villarini A, Pasanisi P, Raimondi M et al (2012) Preventing weight gain during adjuvant chemotherapy for breast cancer: a dietary intervention study. Breast Cancer Res Treat 135:581–589
60. Villarini A, Pasanisi P, Traina A et al (2012) Lifestyle and breast cancer recurrences: The DIANA-5 trial. Tumori 98:1–18
61. Wu AH, Yu MC, Tseng CC et al (2009) Dietary patterns and breast cancer risk in Asian American women. Am J Clin Nutr 89:1145–1154