

Overview

Lifestyle During and After Cancer Treatment

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ABSTRACT:

The aim of this overview was to examine the evidence for links between lifestyle during and after cancer treatment and quality of life, risk of treatment side-effects, rate of progression and prevention of relapse. The reviewed studies were divided into categories according to the role lifestyle plays in progression, during treatment, and in relapse prevention. The evaluated evidence was utilised to show potential lifestyle interventions to facilitate well-being and quality-of-life initiatives. There is now persuasive evidence that dietary choice and exercise can improve the physical and psychological function of patients with cancer. There is also persuasive evidence that lifestyle choice can prevent cancer or the reoccurrence of cancer in susceptible individuals, and possibly improve survival. Thomas, R., Davies N. (2007). *Clinical Oncology* 19, 616–627

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Introduction

Historically, the link between cancer and lifestyle was highlighted by the increased incidence in Asian men and women after migration to North America and Europe, implying environmental factors in addition to genetics alone [1]. Several cohort studies have subsequently confirmed the risks of a stereotypical Western lifestyle, which include high fat and red meat consumption, a low intake of fresh vegetables and fruit, and low levels of exercise [2–4]. Obesity could account for 14% of male and 20% of female cancer deaths in the UK [5,6]. A lack of physical activity is particularly related to colorectal cancer and cohort studies have shown a lower risk in the order of 40–50% compared with those with a sedentary lifestyle [6–8]. The Harvard Center for Cancer Control, for example, estimates that at least 15% of colon cancers could be prevented by 30 min daily exercise [5].

Cynics may argue that lifestyle change after a diagnosis of cancer is analogous to *closing the stable door after the horse has bolted*. On the contrary, emerging evidence shows that lifestyle can influence the rate of cancer progression, improve quality of life, reduce side-effects and risks during therapy, reduce the incidence of relapse, and improve overall survival. Furthermore, there is increasing enthusiasm from patients to be involved in their own management decisions, which in practical terms often concerns diet and lifestyle activities [9]. This paper reviews published evidence for the benefits of an improved lifestyle after a diagnosis of cancer and argues that as oncologists we should be formally introducing lifestyle advice into routine clinical practice.

Lifestyle and Cancer Progression

Nutritional deficiencies and malnutrition are associated with poor tolerance and lower dose intensity and hence indirectly reduce therapeutic outcome [10]. The link between improved lifestyle and better disease response rates is more difficult to prove, but emerging reliable data have been published evaluating patients with indolent or relapsing prostate cancer, where slow progression allows time for alternative interventions [11]. These include a number of epidemiological and cohort studies, which have shown that dietary and lifestyle factors can mediate the transformation of latent prostate cancer into clinically apparent cancers and may influence this process [2–4]. More convincingly, however, are two recent prospective studies that have generated copious media attention [12,13]. The first involved a randomised study of 93 volunteers with early prostate cancer from the USA who had opted not to undergo conventional therapies. They were randomly assigned to intensive nutritional counselling and lifestyle changes, or not, as part of their active surveillance. The lifestyle changes in this study included a vegan diet supplemented with soy, vitamin E, fish oils, selenium and vitamin C, together with a moderate exercise programme and stress management techniques, such as yoga. Prostate-specific antigen (PSA) levels decreased by 4% at 12 months in the intervention group, but increased by 6% in the control group; this was statistically significant ($P < 0.05$). As a secondary end point, serum taken from patients from the intervention group and introduced to prostate cell lines *in vitro* was eight times more likely to inhibit their growth than serum taken

from the control group (70% vs 6%, $P < 0.001$). Furthermore, changes in PSA and cell line growth strongly correlated with the degree of lifestyle change [12].

The second study, a prospective phase II study, evaluated 48 men with PSA relapse after radiotherapy or prostatectomy, comparing PSA doubling time before and after the consumption of about 200 ml pomegranate juice. There was a significant prolongation of PSA doubling time from a mean of 15 months at baseline to 54 months after treatment. As a secondary end point, the patients' baseline oxidative state was significantly lower at baseline and after pomegranate consumption, measured using three separate serum analyses (serum induced proliferation and apoptosis of LNCaP cells, serum lipid peroxidation and serum nitric oxide levels) [13].

Other intervention strategies have focused on the cyclooxygenase-2 (COX-2) pathway, which over-expresses in about 75% of malignancies [14]. In humans, several retrospective and prospective analyses have found an association with the use of non-steroidal anti-inflammatory drugs (NSAIDs) and a lower incidence of prostate, bowel and breast cancers [15–17]. In the UK, a prospective study evaluated dietary intervention supplemented by oral sodium salicylates for its COX properties and copper, manganese gluconates and vitamin C for their antioxidant effects [11]. Within this study, a small cohort of men with progressive early or relapsing prostate cancer had stabilisation of PSA with a mean duration of 17.2 months. It is not clear whether any one of the four components of the supplement was instrumental in this tumour stasis or whether the combination was essential. Also, it is uncertain how much additional benefit was derived from a controlled diet, as it has been reported that people with diets rich in fruit and vegetables, particularly vegetarians, have serum salicylate equivalent to a dose of 80 mg a day — more than enough to inhibit the COX pathway [18]. Whether diet alone, salicylates alone, or a combination of both is the optimal approach remains unanswered [11]. For this reason, a double-blind randomised multicentre controlled trial is underway under the registration of the National Cancer Research Network (NCRN) using a combination of sodium salicylate, diet and supplements in patients with indolent or relapsing prostate cancer. The primary end point, PSA kinetics, is powered to detect a difference between both the control and intervention arms, as well as all patients before and after trial entry [19].

Lifestyle Improving Well-being During and After Cancer Treatment

There is a wealth of information linking good nutritional and exercise interventions with improved tolerability and quality of life during cancer therapy [20]. The most reliable data in this area have addressed the benefits of fatigue, thromboembolism, body composition, psychological well-being and constipation.

Fatigue

Fatigue, reported to be the most common side-effect in 65–90% of patients receiving chemotherapy and in 80–90%

of patients receiving radiotherapy, has been shown to influence a patient's nutritional state, increase morbidity, and negatively affect chemotherapy dose intensity [21]. Regular light exercise has been shown to improve fatigue and quality-of-life issues for patients with cancer, particularly those on chemotherapy [22,23].

Thromboembolism

Thromboembolism remains a significant risk for patients with malignancy, particularly those who are immobile, have undergone a recent surgery, or who are receiving or have previously received chemotherapy [24]. Although strategies such as compression stockings, warfarin and low molecular weight heparin are essential, exercise remains a practical additional aid in reducing this life-threatening complication [25].

Body Composition

Body composition, particularly weight gain during and after adjuvant chemotherapy, is becoming an ever-increasing significant concern. Women with breast cancer, for example, report a 45% incidence of significant weight gain, often at a time in their lives that makes losing it difficult. The reasons are multifactorial, but whatever the cause, prospective exercise intervention studies have shown significant improvement in body fat and lean mass indices [25,26]. Likewise, exercise improves bone mineral density, muscle strength and walking distance, all potential risk factors after chemotherapy [27].

Psychological Well-being

Mood status, depression and anxiety are commonly underdiagnosed in up to 50% of patients with cancer [25]. Cohort studies have suggested that depressed patients with lung and breast cancer have reduced survival compared with patients who are psychologically healthy [28]. A number of prospective exercise intervention studies among patients receiving therapies ranging from chemotherapy, radiotherapy and hormone therapies have shown reduced levels of depression, anxiety and improved quality of life [27,29,30]. In women with breast cancer, continuing exercise into the follow-up period has been shown to improve mood, happiness, self-esteem and energy [31–33].

Constipation

Constipation caused by immobility, opiate analgesics or anti-emetics during chemotherapy remains a significant patient concern. Exercise increases bowel transit time and ameliorates constipation and its associated abdominal cramps [25].

Preventing Relapse

Previously, data on associations between dietary factors and survival from breast cancer have been derived from

follow-up and case–control studies [34,35]. The largest of these is the Nurse’s Health Study in which women with breast cancer completed a dietary questionnaire 1 year after radical therapy. Women following their description of a prudent diet (high fruit, vegetable and fibre; low fat and salt) had a statistically significant lower overall mortality rate compared to those with a typical Western diet. The specific breast cancer mortality overall was not, however, different, except in the comparison of the upper quartile of the prudent diet with the upper quartile of the Western diet and then only in a node-positive subgroup [20].

A subgroup analysis of 4288 patients within the National Surgical Adjuvant Breast and Bowel Project (NSABP) trial between 1989 and 1994 showed that very underweight (body mass index < 19) and obese (body mass index > 35) colon cancer patients had worse overall survival than normal weight patients. This was due to a greater risk of cancer recurrence as well as non-cancer deaths [36]. Similar findings were shown in a retrospective analysis of 1069 men with prostate cancer treated at the Cedars-Sinai Medical Center Los Angeles between 1994 and 2002; obese men had a higher risk of early disease recurrence [37].

A cohort study of 526 cases of colorectal carcinoma showed a 31% reduction in cancer deaths for the physically active compared with the physically inactive across all stages [6]. The benefit was greatest for stage II and III disease, with a hazard ratio for colorectal cancer-specific survival of 0.49 (adjusting for age, sex, and stage) in this subgroup. A similar finding was shown in the CALBG 89803 study in which 816 patients completed detailed lifestyle questionnaires during and after adjuvant chemotherapy for stage III colon cancer. Increased physical activity was associated with improved disease-free and overall survival. In practical terms, this equated to a 35% improvement in disease-free survival for individuals in the highest quintile of regular physical activity compared with the lowest quintile [38].

The most convincing data have been derived from a recent prospective trial that randomised 2437 postmenopausal women with early breast cancer to receive nutritional and lifestyle counselling, or not, as part of routine follow-up. The dietary intervention included eight biweekly individual counselling sessions. Dietary fat intake reduction was significantly greater in the dietary group. After 60 months of follow-up, the breast cancer relapse rate was significantly lower in the intervention group ($P=0.03$). This difference was even greater in the oestrogen receptor-negative subgroup ($P=0.018$). There was a statistically significant improvement in overall survival in the intervention arm, although this was only statistically significant for specific breast cancer recurrence in oestrogen receptor-negative women [39].

Continuing to smoke after a diagnosis of cancer has been shown to increase the risk of further neoplasms, increase complications in surgery, radiation and chemotherapy, impair appetite and nutrition and reduce survival [40–42]. In a retrospective study of 540 patients with histologically confirmed small cell lung cancer, those who stopped smoking at the time of diagnosis had a relative risk of a second lung cancer of 11 (confidence interval 4.4–23), whereas, in those

who continued to smoke it was 32 (confidence interval 12–69) [41]. A further study in patients with lung cancer showed that the chance of survival from the primary disease was double if smoking ceased compared with 40% in patients who continued to smoke [43].

Interaction between Lifestyle and Cancer

Understanding the interaction between lifestyle and cancer is complicated by the caveat that health-seeking enthusiasts often follow a range of behaviours from exercise to dietary manipulation, smoking cessation, reduction in body size, supplements and analgesic intake, confounding the published data [2,3,39]. Many of the underlying mechanisms of benefit or risk remain unproven, but emerging evidence is suggesting an interesting causal relationship with the following categories.

Antioxidants

Antioxidants are thought to wield their anticancer properties by directly or indirectly counterbalancing the superoxide free radicals produced from our diet or other environmental factors [44–47]. Although patients with established cancer have already sustained DNA damage in order to mutate from benign to malignant cells, avoiding further DNA insult may avoid further mutation of indolent malignant or pre-malignant cells into more aggressive phenotypes [2–4]. Otherwise known as free radical scavengers, they are found in a wide variety of dietary sources [2,39].

Carotenoids

Lycopene and beta-carotene are naturally occurring pigments. As well as inducing antioxidant enzymes, there is growing evidence related to cell differentiation and proliferation independent of this mechanism of action [47]. Lycopene, predominant in tomatoes, has been shown to have a protective benefit on prostate cancer risk among US health professionals [45]. For men with established cancer, two small non-randomised studies looked at lycopene and tomato sauce intake and showed decreased PSA progression [44,48]. Beta-carotene, found in carrots and green leafy vegetables, has also shown *in vitro* reduction of proliferation in prostate cancer cell lines [49]. However, trials of supplemented beta-carotene in patients at high risk of lung cancer showed an elevated risk of lung and prostate cancer [50]. Another large chemo-prevention study combined beta-carotene with retinol and showed a lower risk of prostate cancer in those with pre-intervention low plasma levels of beta-carotene; those with high levels had a higher risk [51].

Non-oestrogenic phytochemicals

Non-oestrogenic phytochemicals, or polyphenols, include the phenolic acids, namely benzoic acid (hydroxybenzoic acid, gallic acid) and cinnamic acid (caffeic and quinic acid),

together with the non-oestrogenic flavanoids, including anthocyanidins, the flavanols (catechins and proanthocyanidins), lignans and stilbens. These phytochemicals do not act via a hormonal route, but have been shown to have some direct antioxidative, anti-proliferative activities [4]. Kaempferol, found in teas, broccoli and kale, has particularly been shown to reduce the risk of ovary and breast cancer within the ongoing Nurses' Health Study. These and other phytochemicals are also commonly found in flaxseed, linseeds, nuts, cruciferous vegetables (e.g. cabbage, kale, broccoli), prunes, brightly coloured vegetables, fruits and grains. Antioxidants can be found in less obvious sources such as coffee and chocolate [52], apples used for cider, and the tannin component of red wine [53]. The Food and Drug Administration has published league tables relating to a food's ability to induce these defence enzymes, known as their oxygen radical absorbance capacity [54].

Trace metals and salts

Manganese, copper and zinc are dietary trace elements, classified as antioxidants because they are essential for the production of superoxide dismutase (SOD) and selenium is essential for glutathione peroxidase [4]. Together with catalase these form enzymic defence against carcinogenic oxygen reduction metabolites [55]. It has been postulated that intensive farming food techniques and food processing may reduce these trace metals in our diet [56,57]. There is evidence of an increased risk of carcinogenesis in the presence of copper, manganese or zinc deficiencies, particularly under conditions of high carcinogenic attack where more SOD is needed [2–4,58–61]. Zinc is abundant in many food sources and tends to accumulate more in the prostate. One *in vitro* study suggested that this may offer some protection against prostate cancer cell growth [62]. However, in the Health Professional Follow-up Study, men who took supplemental zinc of more than 100 mg/day or for long durations were more than twice as likely to develop advanced prostate cancer compared with controls [63]. Human prostate cell lines have shown growth inhibition with selenium. This double-blind trial evaluated the benefits of dietary selenium. The primary end point, non-melanoma skin cancer, was not statistically significantly reduced, but the incidence of prostate cancer was significantly reduced [64]. Several large ongoing prostate prevention studies, including the SELECT study, are underway internationally [65,66].

Calcium

Four prospective cohort studies relating to calcium and prostate cancer have been published [3]. Two studies with a mean calcium intake of between 1330 and 1840 mg/day showed no associated risk. Two others, one involving 86 404 men in the Cancer Prevention II (CPII) nutrition cohort, with a mean intake of >2000 mg/day from food and supplements, showed a significantly higher risk of prostate cancer [67]. Five of nine further questionnaire surveys associated a high intake of dairy food with an increased risk

of prostate and breast cancer, but in these surveys a high dairy intake was associated with a high fat intake [3]. Excessive dietary calcium reduces vitamin D, which has shown anti-proliferative benefits that in theory are lost with calcium excess [68].

Oestrogenic Phytochemicals

Phytoestrogens include flavones, isoflavones and flavanones, which are derived in the human diet mainly from soy beans and legumes, including peas, lentils and beans [4]. Dietary intake could potentially create a more favourable hormonal milieu for prostate cancer by inhibiting 5-alpha-reductase, the enzyme responsible for converting testosterone to the more active metabolite dihydrotestosterone [69]. The benefits or risks of phytoestrogenic supplements on breast cancer remain controversial, although this issue may be solved by an ongoing national NCRN *DietCompLfy* study, which is correlating the risks of breast cancer relapse with levels of phytoestrogenic intake [19].

Vitamins

Vitamin A

Vitamin A is a fat-soluble essential vitamin found in fish and dairy food in the preformed isoform retinol. It can also be ingested in fruits and vegetables that contain carotenoid provitamins such as beta-carotene. Prostate cell line data have shown increased apoptosis and reduced proliferation when exposed to synthetic retinoids such as fenretinide [70]. Likewise, in genetically susceptible mice, fenretinide reduced the incidence of prostate cancer by 49% [71]. However, in a subsequent prospective study involving 10 472 US men, no reduction in prostate cancer incidence has yet been shown, although there have only been 93 events in the 5 years of follow-up [72].

Vitamin C

Vitamin C has been shown to prevent the inhibition of gap-junction intercellular communication (GJIC) induced by toxic products such as hydrogen peroxide. The inhibition of GJIC is related to carcinogenesis and tumour promotion [73]. Vitamin C is involved in the mechanism that enables DNA to 'sense' free radicals by integrating with the iron imbedded in DNA, thereby facilitating DNA repair. It is therefore an important factor in immune surveillance against cancer, as according to estimates, each cell in the body can be expected to suffer about 100 000 DNA-damaging events per day [74].

Vitamin D

Vitamin D is converted to the active metabolite calciferol in the kidney. Calciferol exposed to cancer cell lines reduces proliferation, promotes differentiation, inhibits invasion and loss of adhesion [68,75,76] and promotes apoptosis [77]. It has also been shown to interact with the androgen

signalling pathway *in vivo*, inhibiting angiogenesis [70,78]. Clinical studies of calcitriol can dangerously increase serum calcium, but vitamin D analogues have been developed without this risk and are being investigated in an ongoing multicentre study [4].

Vitamin E

Vitamin E in its eight naturally occurring tocopherol isoforms has been linked to a reduction in prostate cancer risk [80]. The Alpha-Tocopherol Beta-Carotene Cancer Prevention Study Trial (ATBC) involving 29 133 male smokers reported a statistically significant reduction in prostate cancer incidence and mortality, although the primary end point of lung cancer was higher [50]. In the Health Professional Follow-up Study, vitamin E intake was also associated with a decreased risk of prostate cancer in smokers, but not overall [79]. The serum-based CII nutrition cohort study showed an inverse correlation between plasma vitamin E levels and prostate cancer, again mainly among smokers and mostly the gamma-tocopherol isoform mainly found in the diet rather than in over the counter supplements [68]. In a further trial involving 39 876 patients with diabetes or cardiovascular disease, alpha-tocopherol showed no reduction in cancer, and the incidence of heart disease was slightly worse [80]. Likewise, in the ATBC study, cerebral haemorrhage risk was also higher in smokers with hypertension who took alpha-tocopherol. The ongoing National Cancer Institute-sponsored double-blind randomised SELECT study comparing selenium and vitamin E supplementation against placebo will provide data on completion in 2013.

Fats

One probable mechanism of benefit for lifestyle changes during cancer relates to a reduction in body fat constitution: associations of adiposity and outcome after cancer treatment have been observed for colorectal cancer [6,38], but also for breast [34,81] and prostate [46] cancer, with the improvement in survival being a result of decreased cancer- and non-cancer-related weight loss [82,83]. The mechanism of risk of being overweight for breast and endometrial cancer may lie in their higher oestradiol levels, which have been reported to reduce after weight reduction programmes [84]. Diet may also influence hormone production and metabolism by a direct action and not via obesity [85,86]. Animal research and case-control studies have shown that diets low in fat and high in fibre are associated with a high excretion of oestrogen in the urine [85,86].

Statins, by chemically reducing fat absorption, may also have a preventive role over and above their ability to reduce cholesterol. Lovastatin and simvastatin have been shown to trigger apoptosis in cancer cell lines [87]. Five randomised trials have shown fewer colon and breast cancers and melanomas in long-term users of statins compared with controls [3]. The data for prostate cancer, however, are inconclusive, as two other large clinical cohort studies did not show a reduced risk with statin intake. A further cohort study of 16 976 subjects showed

a 63% reduction in prostate cancer, although this was not statistically significant [88].

Fat intake, of course, is not all bad; evidence from two large prospective studies [89,90] and a smaller case-control study [91] suggests a protective effect of oily fish intake on cancer incidence and mortality [92]. A unique nutritional component of fish is the long-chain marine omega-3 fatty acids. Cell line xenografts and small human studies have suggested that marine omega-3 fatty acids or the ratio of marine omega-3: omega-6 fatty acids can modulate the COX-2 pathway, a potential route for prostate cancer development [93].

Cyclooxygenase Pathway

The over-expression of COX-2 correlates with a more aggressive phenotype and resistance to hormonal therapies. *In vitro*, inhibitors of COX-2, such as NSAIDs, have been shown to induce apoptosis, inhibit proliferation, impair adhesion and signal angiogenesis in prostate cancer cell lines and xenografts [94]. Ongoing national studies are generally concentrating on pure COX-2 inhibitors, which are thought to avoid the unwanted gastrointestinal COX-1 effects while amplifying the COX-2 effects. The benefits of salicylates in tablet form or those found naturally within the diet have not, however, been established and concerns have arisen with some pure COX-2 inhibitors. First, the reduction in gastrointestinal side-effects of pure COX-2 inhibitors has not been as strong as expected when tested clinically [95]. Second, prospective studies, including a COCHRANE meta-analysis, have shown a reduced incidence of malignancy associated with aspirin rather than other more selective NSAIDs [96–98]. Third, the only prospective randomised clinical studies in oncology published to date showing a protective benefit against recurrent bowel cancer used aspirin [99]. Finally, the cardiac and renal safety of some third generation NSAIDs has more recently been put in doubt [95,100]. As mentioned above, people with diets rich in fruit and vegetables, particularly vegetarians, have serum salicylate equivalent to a dose of 80 mg/day – more than enough to initiate COX's conversion of arachidonic acid to prostaglandins [18]. Also, these patients have a lower incidence of adverse gastrointestinal symptoms. A measure of COX-2 inhibition in further dietary intervention studies would be useful.

Exercise

Theories of the mechanisms of benefit include alterations in prostaglandin levels/ratios and positive effects on the immune system [7,38,101]. For colon cancer, exercise may help by increasing the bowel transit time, reducing the time that potentially carcinogenic substances are in contact with the bowel wall [25]. Exercise and diet also help to control the body's levels of serum lipids and cholesterol; high levels have been particularly associated with a greater risk of advanced disease [102,103]. However, the most compelling emerging evidence lies in the idea that physical activity might exert its beneficial effect via

insulin-like growth factors (IGF) [104,105]. A number of cohort studies have shown an increased risk of cancer, particularly colorectal, with higher levels of IGF-1 and C-peptide. An inverse relationship with insulin-like growth factor binding protein 3 (IGFBP-3) levels [106–109] has also been shown, although this effect has not been confirmed in all studies [110,111]. The benefits of lowering IGF-1 may be linked to its central role in growth regulation processes. The main stimulus for IGF-1 production comes from growth hormone. This stimulatory effect of growth hormone is modulated by insulin, which increases growth hormone receptor levels and in turn IGF-1 [112,113]. Early studies have shown that after binding to its receptors, which are found on normal colonic mucosal cells as well as colon cancer cells, IGF-1 can stimulate cell proliferation, inhibit apoptosis [114] and promote angiogenesis [115,116]. In the circulation, as over 90% of IGF-1 is bound to IGFBP-3, binding inhibits the action of IGF-1 by limiting the availability of free hormone. The most convincing clinical evidence comes from a cohort study of 41 528 people aged between 27 and 75 years with colorectal cancer, recruited

between 1990 and 1994, in which they had previously shown a prognostic benefit of physical activity. This and another large prospective cohort study from Melbourne, Australia, reported statistically lower levels of IGF-1 and higher IGFBP-3 in those physically active before diagnosis and these collated with disease-specific survival and overall survival [117].

Carcinogen Avoidance

Dietary or inhaled chemicals, such as polycyclic aromatic hydrocarbons and aromatic amines, found in super-heated processed or fried foods, are converted to products that can directly or indirectly oxidise water or oxygen into short-lived, but highly energetic, free radicals. These cause double or single DNA strand breaks, allowing cancer-promoting genes to escape from the influence of their suppressor gene guardians [2]. Numerous environmental studies have linked carcinogens to cancers and the USA Food and Drug Administration regularly publishes lists of foods containing high levels of acrylamides and other

Table 1 – Tips to encourage healthy eating in cancer patients

Food	Advice
Reduce saturated fats	Avoid processed fatty foods, cream, and fried foods. Check serum cholesterol and discuss taking a statin if elevated.
Reduce meat intake	Use meat for its taste, preferably not more than once a day. Excess fat should be removed and the meat gently grilled rather than fried to further reduce the fat content and avoid burning. If extra oil needs to be used in cooking, use olive oil rather than animal fat.
Increase all fish intake	All fresh fish, but particularly the oily varieties such as mackerel and sardines. Fresh water fish such as trout have the advantage of avoiding the potential heavy metal contamination of tuna and sword fish, which some suggest should not be eaten more than twice a week.
Reduce exposure to potential carcinogens	Try to avoid heavily processed foods, which often contain high concentrations of fat, salt, sugar and food additives. Reducing the amount of time that vegetables are cooked should maintain the flavour. Wash salads and vegetables thoroughly to avoid pesticides and airborne chemicals, which may have settled on them. Organic foods reduce the pesticide exposure further. Avoid excessive amounts of foods containing high levels of aromatic hydrocarbons and acrylamides, such as smoked food or those associated with high temperature cooking processes such as deep fried foods, crisps, chips, barbecued, and heavily fried meats.
Increase dietary selenium	Brazil nuts, sardines, prawns; 60–75 µg/day; no more than 200 µg/day.
Avoid excessive calcium and zinc	Unless prescribed for other reasons, avoid supplements that give more than 1500 mg of calcium and 11 mg zinc per day.
Increase dietary vitamins	Fresh fruit, raw and calciferous vegetables, grains, oily fish, nuts and salads. Unless you have diarrhoea, try to increase the amount of ripe fruit you eat each day, ideally by eating the whole fruit. Freshly squeezed fruit juices are recommended.
Polyphenols	Onions, leeks, broccoli, blueberries, red wine, tea, apricots, pomegranates, chocolate, coffee, blueberries, kiwis, plums, cherries, ripe fruits, parsley, celery, tomatoes, mint, citrus fruit.
Phytoestrogens	Soybeans and other legumes, including peas, lentils, pinto (baked beans) and other beans and nuts (supplements not recommended).
Non-oestrogenic polyphenols	Skin of colourful foods such as cherries, strawberries, tannins (red wine), blackcurrant, blackberries, dates, cranberries, red grapes, white button mushrooms.
Lignans and stilbens	Flaxseed, linseeds, hemp nuts, grains.
Increase carotenoids (lycopene)	Tomatoes, tomato sauce, chilli, carrots, green vegetables and dark green salads.

Table 2 – Summary of major lifestyle studies after cancer

Study	Participants	Intervention	Results
<i>Randomised</i>			
[12]	93 untreated prostate cancer patients.	Intensive lifestyle intervention or not.	Significant difference in PSA and LNCaP.
[39]	2437 women with early stage treated breast cancer.	Intensive dietary counselling or not.	Lifestyle statistically improved serum fat levels and relapse-free survival.
<i>Prospective non-randomised</i>			
[13]	48 men with PSA relapse after radiotherapy or prostatectomy.	PSA doubling time before and after consumption of about 200 ml pomegranate juice.	Significant reduction in PSA doubling time.
<i>Retrospective analysis of prospective studies</i>			
[20]	2619 women with invasive breast cancer given lifestyle questionnaire 1 year after treatment.	Compared prudent with unhealthy diets.	Lower overall mortality and breast cancer mortality in comparing the uppermost and lowermost quartiles.
[6]	526 patients with treated colorectal cancer.	Via exercise questionnaire; compared physically active with sedentary patients.	Reduction in cancer death in the physically active group.
[38]	816 patients with treated colorectal cancer.	Exercise questionnaire completed before and after chemotherapy.	Reduction in disease-free survival in active group.
<i>Retrospective analysis</i>			
[34]	1982 women treated for breast cancer.	Compared women with good and poor lifestyles.	Women with healthier diets had better survival.
[35]	412 women treated for breast cancer.	Self-reported intake of various dietary factors.	Decreased risk of death from breast cancer in the low fat intake cohort.
[36]	4288 patients treated for colorectal cancer.	Retrospective analysis of the NSABP trial.	Patients with very low BMI < 19 and very high BMI > 35 had worse recurrence rates and overall survival.
[37]	1069 men with treated prostate cancer.	Retrospective analysis of hospital records.	Obese men had earlier PSA recurrence.
[43]	269 head and neck cancer patients.	Retrospective analysis of patient and family lifestyle questionnaires.	Improved disease-free survival in patients who quit smoking.

PSA, prostate-specific antigen; NSABP, National Surgical Adjuvant Breast and Bowel Project; BMI, body mass index.

potential carcinogens, such as pesticides, toxic additives and chemical contaminants [54]. Avoiding carcinogens may, therefore, have a benefit in reducing the risk of developing further cancers in patients who may be more susceptible from a pre-existing genetic signature or damage from chemotherapy or radiotherapy. The latter theory is supported by data from patients surviving the Hiroshima and Nagasaki bombings. A comprehensive medical follow-up of survivors of the atomic bombings by the Radiation Effects Research Foundation showed that those who undertook regular exercise and had a higher intake of fruit and vegetables had a significantly lower risk of cancer, despite their acquired susceptibility [118].

Conclusions

A number of methodological limitations confound the interpretation of the benefits of exercise and diet after a diagnosis of cancer from other risks such as smoking, body

size, supplements and analgesic intake. Nevertheless, despite these caveats there is now persuasive evidence that a healthy lifestyle during and after cancer is associated with improved physical and psychological well-being, reduced risks of treatment, enhanced self-esteem, reduced risk of recurrence and improved survival. Prising the individual anticancer components of a healthy lifestyle will require extensive further evaluation and even then they are probably multifactorial. In the meantime, an important theme emerging from the data is that a simple balanced approach to lifestyle is safer than a faddy supplement-taking culture, as over-consumption of dietary supplements can be unsafe or counterproductive. Ideally, future trial designs should include bespoke patient analysis to identify those individuals with subclinical deficiencies in trace elements and vitamins, which may lead to an increased risk or progression of cancer, especially under circumstances of high carcinogen exposure. The levels and type of dietary supplement for each individual will also probably differ considerably, depending on the patient's dietary

history and genetic susceptibility [119]. As vitamin, mineral and essential fatty acid levels have not always been found to reflect the true status of individual requirements [120] more complex tests may be required in addition to detailed dietary questionnaires. These may include an analysis of a patient's genetic signature [119] measurement of serum metabolites that accumulate in vitamin deficiencies [120] serum lipid peroxide levels as an indicator of oxidative free radical damage [121], or markers relating to the function of the primary defence enzymes, catalase, glutathione S-transferase glutathione and SOD [122].

In the meantime, a logical, albeit pragmatic, approach is summarised in Table 1. This approach is based on the evidence reviewed in this article, some of which is represented in Table 2. It essentially advises adequate amounts of fresh fruits, brightly coloured berries, raw and lightly cooked leafy and cruciferous vegetables, grains, legumes, oily fish, nuts, dark green salads, tomatoes, and soy products. This is complemented with advice to avoid excessive unregulated over the counter supplementation, particularly calcium and zinc at high doses, saturated fat, grilled meats, and other foods with high carcinogen content. Advice on increasing exercise among cancer patients is summarised in Table 3.

How this advice should be formally introduced into clinical practice requires close work with clinicians, patients and advocacy groups. A straightforward first step is to include lifestyle advice sheets in patient information packs after their diagnosis, supported with well-written leaflets. This policy is already adopted by our and a number of UK oncology units. Nurses could be trained to direct patients towards the myriad of council or independent exercise activities available locally and with the Internet, accessible information is even more readily available. Cancernet.co.uk, for example, is able to search for a range of activities by postcode, ranging from ballroom, line and salsa dance lessons, aerobics, yoga and fitness classes, local walking, swimming and cycling groups through to gyms, sport centres, tennis and badminton courts, pilates and personal trainers; information on times, contact numbers and locations is provided. Even if patients do not have access to the Internet, information on these local activities could be printed out as necessary during the patient's treatment pathway.

A more comprehensive, but expensive, strategy is to introduce structured lifestyle clinics facilitated by trained physiotherapists and nutritionists, the feasibility and cost-effectiveness of which are currently under investigation in

Table 3 – Tips to encourage increased exercise activities in cancer patients

Category	Lifestyle advice
Generally	Exercise should not just be a passing fad, but be incorporated into our daily lives for the rest of our lives. During the day we have several choices, which require more or less levels of exertion. Try to take the more active option, such as walking instead of using the car for short journeys or getting off the bus or tube one stop earlier.
Home	If you like exercising at home, it is worth having a semi-formal programme to follow. There are many useful gadgets available to make it more fun (exercise bikes, treadmills, rowing machines, etc). Alternatively, follow an exercise video — there are many good ones available. When watching television, try to get up and walk around for a few minutes at every break.
Office	Use the stairs instead of the lift. If possible take a walk at lunchtime. Try desk exercises — you may look odd, but they can keep you alert, especially when you get tired or sleepy. Do not worry about the comments — people will secretly admire your enthusiasm.
Social life	There is an alternative to the pub or the television. Exercise can and should be sociable and enjoyable — find something that is fun, otherwise you will give it up very quickly.
Walking	In addition to integrating walking into our daily routine, social walking groups are available in many areas and are a good way to meet new people, view interesting scenery and exercise to a variety of ability levels. Golf is a good encouragement to walk and clubs are available throughout Britain for all levels.
Cycling	Cycling socially with family or part of a daily commute, even if only once or twice a week, can be fun and even save money. Consider buying a bike with a basket for the shopping.
Gym	Joining a gym is always a good start. Paying money every month is a good incentive to use it. Even if you are overweight or unfit, do not worry, as so are most other people and nobody of worth will criticise your efforts.
Exercise classes	There are numerous enjoyable ways to exercise in groups at a variety of levels. Your local sports centre will also have many activities from five-a-side football, squash, badminton, volleyball, netball, and numerous exercise aerobics classes.
Swimming	Many pools offer classes to learn to swim; they often offer single sex or disabled classes.
Dance	There are numerous dance classes available in most towns, from traditional ballroom and line dancing to rock and roll or salsa.

Cancernet.co.uk/exercise is able to search for a range of activities by postcode, providing times, contact numbers and locations.

our unit. The rationale for these clinics is that individualised lifestyle counselling will probably elicit a response, especially as fundamental changes in the patient's aspirations and abilities will probably have occurred after their diagnosis and treatment. The cancer itself, surgery, or anticancer therapies may have caused physical disability, fatigue, weight gain and reduced esteem in body image. The baselines or benchmarks patients adopt when evaluating their health status, including the activities they feel they can and cannot participate in, are currently under investigation at our clinic. The theory of health baseline comparisons [123] may influence a patient's adjustment to cancer and lifestyle choices after a cancer diagnosis. If this is the case, there will be scope for the development of more effective, diverse and bespoke lifestyle interventions for cancer patients at diagnosis, during treatment, and on completion of treatment programmes.

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