Full Paper

The role of diet and physical activity in breast, colorectal, and prostate cancer survivorship: a review of the literature

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BACKGROUND: Evidence for the role of diet and physical activity in cancer incidence is well documented, but owing to increased cancer survivorship, an understanding of these lifestyle factors after a cancer diagnosis is of crucial importance. The purpose of this review was to update the literature in a review undertaken for the National Cancer Survivorship Initiative and to include observational studies that were not included in the WCRF survivorship systematic review.

METHODS: Evidence was initially gathered from pre-defined searches of the Cochrane Library Database and PubMed from March 2006 to February 2010. After a comprehensive review regarding lifestyle and cancer, for the purpose of this article, any studies not related to diet and physical activity, prognostic outcomes, and breast, colorectal or prostate cancers were excluded. Another search of 2011 literature was conducted to update the evidence.

RESULTS: A total of 43 records were included in this review. Evidence from observational studies suggests that a low-fat, high-fibre diet might be protective against cancer recurrence and progression. However, there is a paucity of RCTs substantiating this. There is more support for physical activity, with a dose response for better outcomes. When synthesized with findings from the World Cancer Research Fund review of RCTs investigating the effect of diet and physical activity interventions on cancer survival, evidence suggests that the mechanism of benefit from diet and physical activity pertains to body weight, with excess body weight being a risk factor, which is modifiable through lifestyle.

IMPLICATIONS: Cancer survivors would like to have a more active role in their health care and to know how to look after themselves after diagnosis, including what diet and lifestyle changes they should make. The challenge is in integrating lifestyle support into standardised models of aftercare.

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The role of a healthy diet and sufficient physical activity in cancer prevention have been well documented (Chan et al, 2005; Sonn et al, 2005), and it is widely accepted that a poor diet, lack of exercise, smoking and excessive alcohol consumption can increase an individual’s risk of developing cancer. Increasing attention is now being given to the role of lifestyle in cancer survivorship.

There is a growing body of evidence for lifestyle interventions that aim to enhance healthy eating and weight management, and promote physical activity as having the potential to counter some of the adverse effects of cancer treatments, disease progression and other health outcomes (Pekmezci and Demark-Wahnefried, 2011). Besides the potential beneficial effect on recurrence, a healthy diet and regular physical activity may contribute to a reduced risk of comorbid conditions, such as other cancers, cardiovascular disease, diabetes, and so on (Jones and Demark-Wahnefried, 2006).

There have been a number of reviews and meta-analyses that have addressed issues of lifestyle factors and cancer prevention, the most comprehensive possibly being the 2007 report by the World Cancer Research Fund (WCRF), ‘Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective’ (Bekkering et al, 2006). The recommendations from the expert panel are set out in Table 1. The expert panel recommendations on the evidence from the systematic review of RCTs on the effects of nutritional and physical activity interventions on cancer survival concluded that there is emerging evidence that some aspects of food, nutrition, or physical activity (all of which control body weight) may help prevent recurrence (of breast cancer). However, the evidence is not sufficiently developed to enable the panel to make judgements that apply specifically to cancer survivors and are distinct from those for people without cancer (Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective, Chapter 9, Cancer survivors, pp 342–347). More recent specific guidance on diet and physical activity for cancer survivors is becoming available. The British Association of Sport and Exercise Sciences has recently provided guidance on exercise and cancer survivorship (British Sport and Exercise Scientist, 24, Summer 2011), and the American College of Sports Medicine issued guidance on diet/physical activity for cancer survivors in 2010 (Schmitz et al, 2010). These recommendations for diet and physical activity are presented in Table 1, along with the UK recommendations for the general population (Department of Health, Macmillan Cancer Support, NHS Improvement, 2010).
| World Cancer Research Fund/American Institute for Cancer Research (2007) | British Association of Sport and Exercise Sciences (2011) | Department of Health, Physical Activity, Health Improvement, and Protection (UK) (2011) | American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors (2010) |
|---|---|---|---|
| **Body fatness:**<br>Be as lean as possible within the normal range of body weight<br>• Ensure that body weight through childhood and adolescent growth projects towards the lower end of the normal BMI range at age 21 years<br>• Maintain body weight within the normal range from age 21 years<br>• Avoid weight gain and increase in waist circumference throughout adulthood. | Follow health-related physical activity guidelines provided for the general UK population<br>Avoid being sedentary | Adults – 19 – 64 years<br>• Aim to be active daily<br>• Over a week, activity should add up to 150 min (2.5 h) of moderate-intensity activity in bouts of ≥10 min – one way to approach this is to do 30 min on at least 5 days a week<br>• Alternately, comparable benefits can be achieved through 75 min of vigorous-intensity activity spread across the week or a combination of moderate- and vigorous-intensity activity<br>• Undertake physical activity to improve muscle strength on at least 2 days a week<br>• Minimise the amount of time spent being sedentary (sitting) for extended periods. | US DHHS (2008) guidelines on aerobic activity, strength training and flexibility are generally appropriate for cancer survivors<br>• Improve body composition through fat loss for survivors who are obese or overweight<br>• Avoid inactivity and return to normal daily activities as soon as possible after surgery and during adjuvant cancer treatments<br>• The age-appropriate guidelines for aerobic activity are appropriate for cancer survivors; to note a few cancer site-specific elevated risk of skeletal fractures and infection among specific survivors who receive particular treatments |
| **Physical activity:**<br>Be physically active as part of everyday life.<br>• Be moderately physically active, equivalent to brisk walking for at least 30 min a day.<br>• As fitness improves, aim for ≥60 min of moderate or ≥30 min of vigorous physical activity every day.<br>• Limit sedentary habits such as watching television.<br>Limit consumption of energy-dense foods. Avoid sugary drinks<br>• Consume energy-dense foods sparingly<br>• Avoid sugary drinks<br>• Consume ‘fast foods’ sparingly if at all. | Be physically active as part of everyday life.<br>Undertake physical activity to improve muscle strength on at least 2 days a week<br>Minimise the amount of time spent being sedentary (sitting) for extended periods.<br>Consume energy-dense foods sparingly if at all.<br>Limits the intake of red meat and avoid processed meat:<br>• People who eat red meat to consume <500 g (180 z) a week, very little if any to be processed.<br>Limits the consumption of salt. Avoid mouldy cereals (grains) or pulses (legumes):<br>• Avoid salt-preserved, salted or salty foods; preserve foods without using salt.<br>• Limit consumption of processed foods with added salt to ensure an intake of <6 g (2.4 g sodium) a day.<br>• Do not eat mouldy cereals or pulses | Older adults – 65 + years<br>• Older adults who participate in any amount of physical activity gain some health benefits, including maintenance of good physical and cognitive function. Some physical activity is better than none, and more physical activity provides greater health benefits<br>• Be active daily. Over a week, activity should add up to 150 min (2.5 h) of moderate-intensity activity in bouts of ≥10 min – one way to approach this is to do 30 min on at least 5 days a week<br>• For those who are already regularly active at moderate intensity, comparable benefit can be achieved through 75 min of vigorous-intensity activity spread across the week or a combination of moderate and vigorous activity<br>• Undertake physical activity to improve muscle strength on at least 2 days a week<br>• Minimise the amount of time spent being sedentary (sitting) for extended periods.<br>Consume ‘fast foods’ sparingly if at all. <br>Limits the intake of red meat and avoid processed meat:<br>• People who eat red meat to consume <500 g (180 z) a week, very little if any to be processed.<br>Limits the consumption of salt. Avoid mouldy cereals (grains) or pulses (legumes):<br>• Avoid salt-preserved, salted or salty foods; preserve foods without using salt.<br>• Limit consumption of processed foods with added salt to ensure an intake of <6 g (2.4 g sodium) a day.<br>• Do not eat mouldy cereals or pulses | Older adults at risk of falls should incorporate physical activity to improve balance on at least 2 days a week<br>• Avoid salt-preserved, salted or salty foods; preserve foods without using salt.<br>• Limit consumption of processed foods with added salt to ensure an intake of <6 g (2.4 g sodium) a day.<br>• Do not eat mouldy cereals or pulses |

Abbreviation: BMI = body mass index. Recommendations for the Prevention of Cancer, 2007; British Association of Sport and Exercise Sciences, The BASES Statement on Exercise and Cancer Survivorship, first published in Sport and Exercise Sciences, 28, Summer 2011. Start Active, Stay Active. A report on physical activity for health from the four home countries’ Chief Medical Officers; American College of Sports medicine Roundtable on Exercise Guidelines for Cancer Survivors, 2010.
The purpose of this review was to update the literature review undertaken in 2010 for the National Cancer Survivorship Initiative (NCSI) (Davies et al, 2010), which covered evidence on lifestyle and cancer survivorship between 2006 and 2010, and to include observational studies that were excluded from the WRCF survivorship systematic review. A search for literature published between January and August 2011 was undertaken, which confined the search to include only literature for breast, prostate and colorectal cancer survivorship and lifestyle factors of diet and physical activity. The literature from the 2007–2010 review has been retained, which includes only breast, prostate and colorectal studies, and which is focused on diet and physical activity.

Survivorship, for the purpose of this review, was defined according to the definition within the NCSI Vision document (Department of Health, Macmillan Cancer Support, NHS Improvement, 2010). Survivorship encompasses those who are undergoing primary treatment, those who are in remission following treatment, and those who are cured and those with active or advanced disease.

**MATERIALS AND METHODS**

In 2010, as part of the NCSI, a selective review of the evidence for ‘Advising Cancer Survivors about Lifestyle’ (Davies et al, 2010) was conducted. The purpose of this review was to produce evidence that could support professionals in guiding and advising cancer survivors about the need and efficacy of making beneficial lifestyle changes after treatment for curative cancer, as well as to examine evidence published since the WCRF’s ‘A systematic review of RCTs investigating the effect of diet and physical activity interventions on cancer survival’ (Bekkering et al, 2006). Records included within the review covered 2006–2010 and pertained to lifestyle-related factors (such as diet, physical activity, weight, smoking, alcohol consumption) for a number of cancer sites (such as breast, colorectal, lung, prostate cancer, and other tumour sites located as part of the search strategy). Outcomes of interest included prevention, survival, recurrence/progression, symptoms and treatment-related chronic conditions (such as fatigue, lymphoedema, osteoporosis, weight, physical fitness, quality of life, rehabilitation, behavioural change, health and well-being, cost-effectiveness).

For the purpose of this article, those studies related to outcomes other than recurrence and progression were removed, as were those studies related to lifestyle factors other than diet and physical activity. The cancer sites focused on include breast, colorectal and prostate cancers, which have received the greatest preponderance of work from the NCSI. To update the evidence, a further database search was conducted for 2011, the searches being breast OR prostate OR colorectal AND cancer OR neoplasm AND diet* OR exercise OR physical activity OR weight OR lifestyle. Records were eligible if they met the following inclusion criteria: (1) lifestyle-related – diet or physical activity; (2) cancer sites: breast, colorectal or prostate; (3) trajectory – during primary cancer treatment or post-primary treatment; (4) outcomes of interest – survival, recurrence/progression; (5) adult population. Eligibility assessment was performed independently by three reviewers, with any disagreements between reviewers being resolved by consensus. Selection criteria were based on the PRISMA statement (Moher et al, 2009), which places systematic reviews, meta-analyses and RCTs as being ‘gold standard’ for evidence quality. Some studies before the initial search for 2006 records have been included, where the evidence offers further insights into those outcomes being examined.

Details of the studies included in this review (e.g., sample size, primary outcomes) are presented in Tables 2–5, along with the adjusted hazard ratio (HR) or relative risk, 95% confidence interval (95% CI), and significance levels. Diet, supplements and physical activity are presented separately for each of the three cancer sites being evaluated in this review.

A total of 43 records (Figure 1) were included in this review. In synthesising the evidence obtained from these records, site-specific findings are reported for breast, colorectal and prostate cancers. Where relevant, the evidence within the WCRF review is referred to, followed by additional evidence identified within the current review.

**RESULTS**

**Diet**

Recommendations for diet comprise guidance on limiting consumption of energy-dense foods with a high sugar or fat content (Table 1). The consumption of plant-based foods including fruit, vegetables and whole grains is recommended. Caution has also been raised against foods that are high in salt, including processed meats and mouldy cereals or pulses. The body of evidence from observational studies do increasingly indicate that obesity is a modifiable risk factor for both breast and colorectal cancer progression and survival (Patterson et al, 2010; Sinicrope et al, 2010).

Table 2 presents evidence obtained on diet for breast cancer from two large-scale multicentre RCTs – the Women’s Intervention Nutrition Study (WINS) and the Women’s Healthy Eating and Living (WHEL). These two large-scale studies (WINS, n = 2437 and WHEL, n = 3088) and the numerous subsequent secondary analyses are included in this review because of the significance of their dietary data and conflicting outcomes. Even after an in-depth critique of the methods and interpretation of the WINS and WHEL outcomes, Patterson et al (2010), in their recent review of physical activity, diet and adiposity, and female breast cancer prognosis, concluded that data from these trials indicate that in a general population of breast cancer survivors, dietary interventions without weight loss or physical activity are not sufficient to improve breast cancer prognosis. Table 3 presents all other evidence obtained on diet for breast, colorectal, and prostate cancers.

**Breast cancer** Evidence for the role of dietary fat in breast cancer progression and survival was variable in the current review. A large prospective study (n = 90 655) with an 8-year follow-up found that dietary fat does increase the risk of recurrence or death in pre-menopausal women (Cho et al, 2003). These findings have been supported by the large multicentre prospective RCT, WINS, which found a protective benefit of a reduced-fat dietary intervention (Chlebowski et al, 2006). This protective benefit was more prominent in women diagnosed with hormone-receptor-negative breast cancer (n = 2437). In this RCT, women were randomised to either a dietary intervention comprising a reduction in the percentage of calories from fat to 15% or a control group comprising standardised dietary guidelines. The hazard ratio (HR) of recurrence in the intervention group compared with the control group was 0.76 (95% CI = 0.60–0.98; P = 0.077). Furthermore, in 362 women with estrogen receptor (ER) and progesterone receptor (PR) disease, a significant overall survival (OS) benefit was seen in the intervention group (7.5% vs 18.1%, cumulative mortality) (Chlebowski et al, 2008). A subgroup analysis of 53 women revealed that elevated insulin concentrations may be influenced by dietary fat reduction (P > 0.05) (Khaodhiar et al, 2003). These findings point to the possibility that the mechanism of benefit obtained from a low-dietary-fat diet might be through its mediating effect on metabolic hormones such as insulin.

As low-fat diets are often accompanied by high intakes of fruit and vegetables, various components of a diet comprising high levels of fruit and vegetables have been investigated. Carotenoids...
Chlebowski et al (2006) | Interim analysis of a randomised, prospective, multicentre clinical trial (WINS) to test the effect of a dietary intervention designed to reduce fat intake. Randomisation was to: (1) Dietary intervention: reduce percentage of calories from fat to 15%. The low-fat eating plan was initiated during 8 biweekly individual, in-person counselling sessions, each lasting 1.5 h. Dietician 3 monthly, with optional monthly dietary group sessions. (2) Control group: one baseline dietician visit and contacts every 3 months thereafter. Written information provided on general dietary guidelines and counselling on nutritional adequacy for vitamin and mineral intake only | Breast cancer patients (n = 2437) | Mean = 60 months (5 years) | Relapse-free survival; overall survival | A total of 277 relapse events have been reported in 96 of 975 (9.8%) women in the dietary group and 181 of 1462 (12.4%) women in the control group. The HR of relapse events in the intervention group compared with the control group was 0.76 (95% CI = 0.60–0.98, P = 0.077 for stratified log rank and P = 0.034 for adjusted Cox model analysis) |

Chlebowski et al (2008) | A protocol-mandated survival analysis update to the interim analysis of WINS | Breast cancer patients (n = 2437) | 7 years | Overall survival | Although fewer deaths were seen in the intervention group, this was not statistically significant. In 362 women with ER and (progesterone receptor) PR disease, a significant overall survival benefit was seen in the intervention group (7.5 vs 18.1%, cumulative mortality) |

Dwyer et al (2008) | A subanalysis of participants in the WINS trial to determine whether differences existed in dietary intakes of flavonoids among WINS women who had been randomised to the very-low-fat diet after they modified their eating habits to achieve their goals. Comparisons were made between the intervention and control groups on intakes of total flavonoids and six flavonoid classes (isoflavones, flavones, flavanones, flavonol, flavan-3-ols and anthocyanins) using the US Department of Agriculture food flavonoid database and a flavonoid dietary supplement database on three 24-h dietary recalls at baseline and 12 months after randomisation | Randomly selected breast cancer patients (n = 550; 218 from the dietary intervention and 332 from the control group) | 12 months of intervention | Disease-free survival | After 12 months of intervention, with 39 participants lost to follow-up, flavonoid intakes remained similar in both groups (201 ± 252 s.d. mg per day, n = 316 in the usual diet group vs 235 ± 425 s.d. mg per day, n = 195 in the very-low-fat group; P = NS). In this random sample of WINS participants, neither total flavonoid intakes nor intakes of subclasses of flavonoids differed between those who had dramatically decreased their fat intakes and those who had not. Flavonoid intakes are therefore unlikely to account for WINS results |

Khaodhiar et al (2003) | Subgroup analysis of WINS participants (Chlebowski et al, 2006), examining relationships between dietary intake and insulin resistance | 53 women from 3 clinical sites | 2 years after commencing intervention | Insulin resistance | Of those women with initial insulin resistance, after 1 year, women in the intervention group saw their fasting insulin decrease by 18 ± 34 μU/ml−1; in comparison, fasting insulin of women in the control group decreased by only 13.8 ± 47 μU/ml−1. Although not quite statistically significant, these results predict that elevated insulin concentrations may be influenced by dietary fat reduction |

WHEL Pierce et al (2007) | The multicentre WHEL RCT. Participants randomised to: (1) An intensive telephone counselling intervention: promoting a daily dietary intake of 5 vegetable servings, 16 oz of vegetable juice, 3 fruit servings, 30 g fibre and 15–20% of energy from fat. (2) Control group: received printed materials (but no counselling) promoting the five-a-day guidelines of daily intakes of 5 servings of fruit and vegetables, >20 g of fibre and <30% of energy from fat | Breast cancer (n = 3088) | After 7 years of intervention | Invasive breast cancer incidence or recurrence; death from any cause | There were no additional health benefits of dramatically increasing intake of nutrient-rich plant-based foods, relative to the comparison group |
have received particular attention, with past evidence suggesting that carotenoids do have a role in survival (Ingram, 1994). More recent prospective longitudinal RCTs have found this not to be the case, such as the WHEL RCT (Pierce et al, 2007). In the WHEL trial, women \( (n = 3088) \) were randomised to either an intensive telephone-counselling intervention promoting daily dietary intake of 5 vegetable servings, 16 oz vegetable juice, 3 fruit servings, 30 g fibre and 15–20% of energy from fat, or a control group promoting the five-a-day guidelines of daily intakes of 5 servings of fruit and vegetables, >20 g of fibre and <30% of energy from fat. There were no additional health benefits of dramatically increasing intake of nutrient-rich plant-based foods relative to the control group. However, as pointed out by Patterson et al (2010), it is possible that the level of dietary change achieved in both the WINS and WHEL interventions was not sufficient to change cancer prognosis, or that the wrong dietary components were being examined.

When Gold et al (2009) conducted a secondary analysis of 2967 participants in the WHEL RCT, it was found that hot flush (HF)-negative women in the intervention had 31% fewer events than did HF-negative women in the control group over 7.3 years of follow-up. Among HF-negative post-menopausal women, the intervention effect was even stronger, with a 47% reduction in risk compared with HF-negative women assigned to the comparison group. Compared with HF-negative women in the comparison group, women with baseline HFs had a lower risk of additional breast cancer events, regardless of whether they were randomly assigned to the dietary intervention group or to the comparison group.

### Table 2 (Continued)

| Author | Study design/intervention | Sample/ inclusion | Follow-up period | Primary outcome | Results |
|--------|---------------------------|-------------------|------------------|----------------|---------|
| Thomson et al (2007) | Subanalysis of a purposive sample of participants in the WHEL RCT (see Gold et al, 2009 in this table) | Breast cancer patients \( (n = 207) \) | Not reported | Oxidative stress | Dietary carotenoid levels were not significantly associated with oxidative stress, although dietary lycopene and lutein/zeaxanthin were modestly associated with 8-OHdG levels \( (P = 0.054 \) and 0.088, respectively). Key findings include a significant inverse association between total plasma carotenoid concentrations and oxidative stress as measured by urinary 8-OHdG and a moderately significant inverse association with 8-iso-PGF2α, a protective association that was not shown for dietary carotenoid intake |
| Gold et al (2009) | Secondary analysis of a purposive sample of WHEL participants, to determine whether a low-fat diet high in vegetables, fruit and fibre affects prognosis in breast cancer survivors with or without HFs after treatment | 2967 women whose baseline HF severity report in the previous 4 weeks was available | 7.3 years into the intervention | Additional breast cancer events and death from any cause | HF-negative women in the intervention had a 31% lower event rate than did HF-negative women in the comparison group over 7.3 years of follow-up; among HF-negative post-menopausal women, the intervention effect was even stronger, with a 47% reduction in risk compared with HF-negative women assigned to the comparison group. Compared with HF-negative women in the comparison group, women with baseline HFs had a lower risk of additional breast cancer events, regardless of whether they were randomly assigned to the dietary intervention group or to the comparison group |
| Caan et al (2011) | Examination of data from the WHEL study, to explore the effect of soy intake on breast cancer prognosis. Isoflavone intakes were measured after diagnosis by using a food-frequency questionnaire. Women self-reported new outcome events semi-annually, which were then verified by medical records and/or death certificates | 3088 breast cancer survivors, diagnosed between 1991 and 2000 with early-stage breast cancer | Median of 7.3 years | Breast cancer-related mortality | As isoflavone intake increased, risk of death decreased \( (P \) for trend = 0.02). Women at the highest levels of isoflavone intake (>16.3 mg isoflavones) had a non-significant 54% reduction in risk of death |

Abbreviations: CI = confidence interval; ER = oestrogen receptor; HF = hot flush; HR = hazard ratio; NS = non-significant; RCT = randomised controlled study; WHEL = Women’s Healthy Eating and Living; WINS = Women’s Intervention Nutrition Study.
Table 3  Diet evidence

| Author | Study design/intervention | Sample/inclusion | Follow-up period | Primary outcome | Results |
|--------|---------------------------|------------------|------------------|----------------|---------|
| Belle et al (2011) | Health, Eating, Activity, and Lifestyle (HEAL) study: Investigation into the associations of dietary fibre, carbohydrates, glycemic index (GI) and glycemic load (GL) with breast cancer prognosis. Usual diet was assessed with a food-frequency questionnaire. Cox proportional hazards regression estimated multivariate-adjusted hazard ratios and 95% confidence intervals (95% CI) | n=688 stage 0 to IIA breast cancer survivors | Median of 6.7 years after diagnosis | Total mortality, breast cancer mortality, non-fatal recurrence and second occurrence data were obtained from SEER (Surveillance, Epidemiology, and End Results) registries and medical records. There was an inverse association between fibre intake and mortality. Multivariate-adjusted hazard rate ratios (HRR) comparing high with low intake were 0.53 (95% CI = 0.23 – 1.23) and 0.75 (95% CI = 0.43 – 1.31). A threshold effect was observed whereby no additional benefit was observed for intakes of ≥9 g per day. Fibre intake was inversely associated with breast cancer-specific mortality (HRR = 0.68, 95% CI = 0.27 – 1.70) and risk of non-fatal recurrence or second occurrence (HRR = 0.68, 95% CI = 0.27 – 1.70), but results were not statistically significant. | Soy intake pre-diagnosis was unrelated to disease-free breast cancer survival (HRR = 0.99, 95% CI = 0.73 – 1.33 for the highest tertile compared with the lowest tertile) |
| Boyapati et al (2005) | The Shanghai Breast Cancer Cohort Study. Examining associations between soy and breast cancer survival | 1459 breast cancer patients | 5.2 years | Disease-free survival | Relative to women in the lowest quintile of fat intake, women in the highest quintile of intake had a slightly increased risk of breast cancer (RR = 1.25, 95% CI = 0.98 – 1.59; P = 0.06). The increase was associated with intake of animal fat but not vegetable fat; RRs for the increasing quintiles of animal fat intake were 1.00 (referent), 1.28, 1.37, 1.54 and 1.33 (95% CI = 1.02 – 1.73; P = 0.002) |
| Cho et al (2003) | A prospective analysis of the relationship between dietary fat intake and breast cancer risk among pre-menopausal women (Nurses’ Health Study) | Pre-menopausal women (n = 90,655), aged between 24 and 46 years when recruited in 1991 | 8 years after recruitment (1991 – 1999) | Fat intake was assessed with a food-frequency questionnaire at baseline in 1991 and again in 1995 | Women with deficient vitamin D levels had an increased risk of distant recurrence (HR = 1.54, 95% CI = 1.16 – 2.32) and death (HR = 1.73, 95% CI = 1.05 – 2.86) compared with those with sufficient levels |
| Goodwin et al (2009) | Prospective cohort study examining the influence of vitamin D on breast cancer prognosis | 512 women with early breast cancer | Mean = 11.6 years | Cancer recurrence and mortality | The multiple odds ratio (OR) for treatment failure in women with E-rich tumours was 1.08 for each 1% increase in percentage of total energy (%E) from total fat. For treatment failure within the first 2 years, the OR was 1.19 for each 1-mg increase in vitamin E intake per 10 MJ of energy. No association between dietary habits and treatment failure was found for women with ER-positive cancers |
| Holm et al (1993) | Interviews regarding diet history, to determine whether dietary habits are associated with disease-free survival in patients with breast cancer who have undergone treatment | 240 women with stage I–II breast cancer (50 – 65 years) | 4 years | Disease-free survival | At high levels of consumption, there were significantly fewer deaths from breast cancer only I in the group of highest b-carotene consumers compared with 8 in the intermediate group and 12 in the lowest group (trend P = 0.0012). Equivalent figures for vitamin C were 3, 7 and 11 deaths for the highest, intermediate and lowest consumption groups, respectively (trend P = 0.0286) |
| Ingram (1994) | Cohort study evaluating the role of vitamins in breast cancer mortality | 103 women 3 months after operation | Mean = 81 months | Mortality from breast cancer | The HR and 95% CI of death in the highest tertile compared with the lowest tertile of total fat, fibre, vegetable and fruit intake was 3.12 (95% CI: 1.79 – 5.44), 0.48 (95% CI: 0.27 – 0.86), 0.57 (95% CI = 0.35 – 0.94) and 0.63 (95% CI = 0.38 – 1.05), respectively (P<0.05 for trend, except for fruit intake). Intakes of other nutrients, including fat, vitamin C and carotenoids, were also significantly associated with reduced mortality (P<0.05 for trend) |
| McEligot et al (2008) | Retrospective study into the influence of diet on overall survival in women with breast cancer | Post-menopausal breast cancer survivors (n = 516) | Mean = 80 months after diagnosis | Death due to any cause | One study was identified comparing prudent vs. Western dietary pattern (Kwan et al, 2009). Overall, there were 12 studies of macronutrients and dietary patterns with mortality as an outcome, 4 of which meet the inclusion criteria of the current review but were not identified by the search strategy (Borugian et al, 2004; Barnett et al, 2008; Dal Maso et al, 2008). For the 3 studies on carbohydrates (Holmes et al, 1999; Borugian et al, 2004; McEligot et al, 2006) findings were mixed, with 1 report of a statistically significant protective effect (McEligot et al, 2006) the | |
Table 3 (Continued)

| Author          | Study design/Intervention                                                                 | Sample/inclusion                                                                 | Follow-up period | Primary outcome                                                                 | Results                                                                 |
|-----------------|------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|------------------|--------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Colorectal      | Prospective observational study to determine the association of dietary patterns with cancer recurrences and mortality of colon cancer survivors | 1,009 patients with stage III colon cancer who were enrolled in an adjuvant chemotherapy RCT between April 1999 and May 2001 | Median <= 53 years. Patients were followed up for cancer recurrence or death | Disease-free survival, recurrence-free survival and overall survival by dietary pattern | 324 patients had cancer recurrence, 223 patients died with cancer recurrence and 28 died without documented cancer recurrence. Two major dietary patterns, prudent and Western, were identified by factor analysis. The prudent pattern was characterised by high intakes of fruit and vegetables, poultry, and fish; and the Western pattern was characterised by high intakes of meat, fat, refined grains, and dessert. A higher intake of a Western dietary pattern after cancer diagnosis was associated with a significantly worse disease-free survival (colon cancer recurrences or death). Compared with patients in the lowest quintile of Western dietary pattern, those in the highest quintile experienced an adjusted hazard ratio (AHR) for disease-free survival of 3.25 (95% CI = 2.04 – 5.19; P for trend <0.001). The Western dietary pattern was associated with a similar detriment in recurrence-free survival (AHR = 2.85; 95% CI = 1.75 – 4.63) and overall survival (AHR = 2.32; 95% CI = 1.36 – 3.96), comparing highest with lowest quintiles (both with P for trend <0.001). The reduction in disease-free survival with a Western dietary pattern was not significantly modified by sex, age, nodal stage, body mass index, physical activity level, baseline performance status, or treatment group. In contrast, the prudent dietary pattern was not significantly associated with cancer recurrence or mortality. |
| Prostate        | An RCT with participants being randomised to a 4-week low-fat diet group or a Western diet group. Feeding study with the low-fat diet defined as < 15% of total energy from fat and the Western diet defined as 40% of energy coming from fat | 18 men diagnosed with prostate cancer within the past 2 years and on active surveillance (mean age = 64 years) | Immediately after the 4-week intervention | Fasting serum was collected at baseline and after the intervention to measure prostate-specific antigen, sex hormones, insulin, insulin-like growth factor I and II, insulin-like growth factor-binding proteins, lipids and fatty acids. LNCaP cells (ATCC(R)) were cultured in medium containing pre-intervention and post-intervention human serum to assess the in vitro effect of the diet on prostate cancer cell proliferation | Serum from men in the low-fat group significantly decreased the growth of LNCaP cells relative to Western diet serum (P = 0.03). There were no significant between-group changes in serum prostate-specific antigen, sex hormones, insulin, insulin-like growth factor I and II, and insulin-like growth factor-binding proteins. Serum triglyceride and linoleic acid (omega-6) levels were decreased in the low-fat group (P = 0.031 and P = 0.005, respectively). Correlation analysis revealed that decreased omega-6 and increased omega-3 fatty acid correlated with decreased serum stimulated LNCaP cell growth (r = 0.64, P = 0.004, and r = –0.49, P = 0.04, respectively). |
| Author                  | Study design/intervention                                                                 | Sample/inclusion         | Follow-up period | Primary outcome                  | Results                                                                                                                                                                                                 |
|------------------------|------------------------------------------------------------------------------------------|--------------------------|-----------------|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Heymach et al (2011)   | Exploration of the effect of diet on angiogenesis and inflammation, which are central to tumour growth and progression. Changes in 30 plasma cytokines and angiogenic factors (CAF) were explored in prostate cancer patients enrolled in a pre-operative, randomised controlled phase II trial with four arms: control (usual diet); low-fat (LF) diet; flaxseed-supplemented (FS) diet and flaxseed-supplemented, low-fat diet. The mean duration of dietary intervention was 30–31 days. | 145 men with prostate cancer | N/A             | Changes in CAFs                  | Compared with the control arm, 6 CAFs including pro-angiogenic factors (stromal-cell derived-1-x and myeloid factors, granulocyte colony-stimulating factor, macrophage colony-stimulating factor) all decreased in the LF arm compared with controls; 3 and 4 CAFs changed in the FS and FS+LF arms, respectively. These results suggest that a low-fat diet without flaxseed may reduce levels of specific inflammatory cytokines and angiogenic factors and suggests that the NF-κB pathway may be a mediator of these changes |
| Hori et al (2011)      | A review exploring the current evidence for the role of different dietary components and its effect on prostate cancer prevention and progression. A literature search was conducted using PubMed to identify key studies. RCTs were favoured over observational studies. Results from systematic reviews or a meta-analysis of RCTs/observational studies were given preference to quoting individual studies. | Prostate cancer           | N/A             | Prevention and progression       | There was some evidence suggesting green tea, isoflavone, lycopene, cruciferous vegetable and omega-3 polyunsaturated fatty acid intake to be beneficial in the prevention and/or progression of prostate cancer. There was also evidence suggesting that a high total fat, meat (especially well-cooked) and multivitamin intake may be associated with an increased risk of developing prostate cancer; more research is required to establish its effect on progression |
| Parsons et al (2008)   | Part of the Men’s Eating and Living (MEAL) Study (a multicentre pilot trial of a diet-based intervention for prostate cancer). A theory-based telephone counselling intervention vs standardised written materials. The intervention group were counselled to consume at least seven servings of vegetables per day (two cruciferous, two tomato products and three others), two servings a day of whole grains and one serving a day of beans/legumes. Telephone counselling comprised 13 (25–50min) sessions over 6 months. | 43 prostate cancer survivors on active surveillance (mean age = 64 years) | 6 months         | Dietary intakes and plasma carotenoid levels were assessed at baseline and after 6 months                                             | In the intervention group, the mean daily intakes of total vegetables, crucifers and tomato products increased by 71%, 180% and 26%, respectively (P < 0.05); in the control group, there were no significant changes in mean intakes of these components. Similarly, in the intervention arm, mean plasma levels of α-carotene, β-carotene, lutein, lycopene and total carotenoids increased by 37%, 32%, 23%, 30% and 25%, respectively (P < 0.05); in the control group, there were no significant changes in plasma levels of these components. There were no significant changes in either group in whole grain, beans/legumes or fat intake |
| Richman et al (2010)   | A prospective study of the association between post-diagnostic consumption of processed and unprocessed red meat, fish, poultry and eggs, and the risk of prostate cancer recurrence or progression. | 1294 men with prostate cancer, without recurrence or progression as of 2004–2005, who were participating in the Cancer of the Prostate Strategic Urologic Research Endeavour | Mean = 2 years |                                                                                                | Intakes of processed and unprocessed red meat, fish, total poultry and skinless poultry were not associated with prostate cancer recurrence or progression. Greater consumption of eggs and poultry with skin was associated with twofold increases in risk in a comparison of extreme quantiles: eggs (HR = 2.02; 95% CI = 1.10 – 3.72; P for trend = 0.05) and poultry with skin (HR = 2.26; 95% CI = 1.36 – 3.76; P for trend = 0.003). An interaction was observed between prognostic risk at diagnosis and poultry. Men with high prognostic risk and a high poultry intake had a fourfold increased risk of recurrence or progression compared with men with low/intermediate prognostic risk and a low poultry intake (P for interaction = 0.003). The findings suggest that the post-diagnostic consumption of processed or unprocessed red meat, fish or skinless poultry is not associated with prostate cancer recurrence or progression, whereas consumption of eggs and poultry with skin may increase the risk |

Abbreviations: CI = confidence interval; ER = oestrogen receptor; HR = hazard ratio; N/A = not applicable; RCT = randomised controlled trial; RR = relative risk.
| Author               | Study design/intervention                                                                 | Sample/ inclusion          | Follow-up period | Primary outcome                        | Results                                                                 |
|----------------------|-------------------------------------------------------------------------------------------|----------------------------|------------------|----------------------------------------|-------------------------------------------------------------------------|
| **Supplements**      |                                                                                           |                            |                  |                                        |                                                                         |
| Breast              | Reschauer et al (2003) Case–control study testing the hypothesis that antioxidant supplements may reduce the risk of breast cancer recurrence or mortality | 385 post-menopausal women with breast cancer | 12–14 years      | Breast cancer recurrence or death      | Antioxidant supplement users compared with non-users were less likely to have a breast cancer recurrence or breast cancer-related death (OR = 0.54, 95% CI = 0.27–1.04). Vitamin E supplements showed a modest protective effect when used for > 3 years (OR = 0.33, 95% CI = 0.10–1.07). Risks of recurrence and disease-related mortality were reduced among women using vitamin C and vitamin E supplements for > 3 years. |
| Patterson et al      | A review of the published epidemiological research on lifestyle and breast cancer outcomes. Research included RCTs, cohort studies, or case–control studies of breast cancer outcomes. Included studies had been published in the previous 10 years (1999–2009), as well as a few large studies published > 10 years ago. Papers were included only if there were at least 500 participants. Studies of exposure biomarkers such as serum nutrient concentrations were not included, nor were studies with intermediate markers of breast cancer (e.g., mammographic density) or non-invasive lesions (e.g., ductal carcinoma in situ) | Breast cancer              | Not reported      | Additional breast cancer events and mortality | There were only four studies of micronutrients and/or fruit and vegetables with mortality (Jain et al, 1994; Holmes et al, 1999; McEligot et al, 2006; Dal Maso et al, 2008), although these publications typically included many exposures. For example, Holmes et al reported on 93 dietary exposures in relation to all-cause mortality (of which 17 were statistically significant). Overall, the HRs showed a trend towards being protective. Among the vitamins, minerals, fruit, and vegetables in this review, statistically significant protective associations were seen for higher intakes of calcium (Holmes et al, 1999), vitamin C (Jain et al, 1994), and vegetable consumption (McEligot et al, 2006). Given the limited number of total studies and the multiplicity of dietary exposures reported in each study, it was not considered appropriate to calculate a weighted average for the exposures presented in the review. |
| Ng et al (2008)      | Nurses’ Health Study prospective examination of the association between pre-diagnosis 25(OH)D levels and mortality in colorectal cancer patients | 304 colorectal cancer patients | Mean = 78 months | Colorectal cancer mortality            | Higher plasma 25(OH)D levels were associated with a significant reduction in overall mortality (P for trend = 0.02). Compared with the lowest quartile, participants in the highest quartile had an adjusted HR of 0.52 (95% CI = 0.29–0.94) for overall mortality. A trend towards improved colorectal cancer-specific mortality was also seen (HR = 0.61; 95% CI = 0.31–1.19). |
| Ng et al (2010)      | A prospective, observational study. Patients reported on multivitamin use during and 6 months after adjuvant chemotherapy. Patients were observed until March 2009 for disease recurrence and death. To minimise bias by occult recurrence, patients who had a recurrence or died within 90 days of their multivitamin assessment were excluded | 1038 patients with stage III colon cancer enrolled in a randomised adjuvant chemotherapy trial | 6 months after adjuvant chemotherapy | Cancer-specific and overall mortality | Among 1038 patients, 518 (49.9%) reported multivitamin use during adjuvant chemotherapy. Compared with non-users, the multivariate HR for disease-free survival was 0.94 (95% CI = 0.77–1.15) for patients who used multivitamins. Similarly, multivitamin use during adjuvant chemotherapy was not significantly associated with recurrence-free survival (multivariate HR = 0.93; 95% CI = 0.75–1.15) or overall survival (multivariate HR = 0.92; 95% CI = 0.74–1.16). Neither an increasing number of tablets nor increasing duration of use before cancer diagnosis was associated with cancer recurrence or mortality. Multivitamin use also did not improve the rates of grade 3 and higher GI toxicity. |
| Author                  | Study design/intervention                                                                 | Sample/inclusion     | Follow-up period | Primary outcome                                                                 | Results                                                                                                                                 |
|------------------------|-------------------------------------------------------------------------------------------|----------------------|------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Prostate               | Phase II trial testing the comparative effects of flaxseed supplementation with and without a low-fat diet. Controls continued usual diet. The flaxseed group received 30g per day of ground flaxseed. The low-fat group received instructions on a diet of <20% of kcal from fat. The study was conducted for a mean of 30 days. | 161 men with operable prostate cancer scheduled for prostatectomy (mean age = 59.2 years) | Urine analysed for presence of lignans to confirm flaxseed consumption. | Prostate cancer-specific mortality was significantly lower (P < 0.002) among men in the flaxseed group. Men in the low-fat group had a significant decrease in serum cholesterol (P = 0.048). |
| Epstein et al (2011)   | Swedish population-based cohort study examining whether dietary zinc assessed near the time of prostate cancer diagnosis is associated with improved disease-specific survival. | 525 men aged <80 years with a diagnosis of prostate cancer made between 1989 and 1994 | Median follow-up of 6.4 years | Study participants completed self-administered food-frequency questionnaires, and zinc intake was derived from nutrient databases. | High dietary zinc intake was associated with a reduced risk of prostate-specific mortality (HR_Q4 vs Q1 = 0.64; 95% CI = 0.44 – 0.94; P for trend = 0.05) in the study population. The association was stronger in men with localised tumours (HR = 0.24; 95% CI = 0.09 – 0.66; P for trend = 0.005). Zinc intake was not associated with mortality from other causes. |
| McLarty et al (2009)   | An investigation into the effects of short-term supplementation with the active compounds in green tea on serum biomarkers in patients with prostate cancer. | 26 men with prostate cancer | Not reported | PSA levels | Biomarkers of prostate cancer decreased significantly, including total protein, albumin, aspartate aminotransferase, alkaline phosphatase and amylase. |
| Ornish et al (2005)    | RCT exploring lifestyle changes including a vegan diet supplemented with soy, vitamin E, fish oils, selenium and vitamin C, together with a moderate physical activity programme and stress management. | Men with early prostate cancer (n = 93) | 12 months into the intervention | PSA and serum stimulated LNCaP cell growth | PSA levels decreased by 4% at 12 months in the intervention group, but increased by 6% in the control group; this was statistically significant and strongly correlated with the degree of lifestyle change. The growth of LNCaP prostate cancer cells was inhibited almost 8 times more by serum from the intervention group compared with the control group (70 vs 9%, P < 0.001). |
| Pantuck et al (2006)   | Phase II, two-stage clinical trial to determine the effects of pomegranate juice on PSA levels. | 46 men with increasing PSA levels, post-treatment (surgery or radiotherapy) | Every 3 months for 54 months | PSA levels | Mean PSA doubling time significantly increased with treatment from a mean of 15 months at baseline to 54 months after treatment (P < 0.0001). In vitro assays comparing pre-treatment and post-treatment patient serum on the growth of LNCaP showed a 12% decrease in cell proliferation and a 17% increase in apoptosis (P = 0.0048 and 0.0004, respectively), a 23% increase in serum nitric oxide (P = 0.0085) and significant (P < 0.02) reductions in oxidative state and sensitivity to oxidation of serum lipids after vs before pomegranate juice. |

Abbreviations: CI = confidence interval; HR = hazard ratio; GI = gastrointestinal; OR = odds ratio; RCT = randomised controlled trial.
Table 5 Physical activity evidence

| Author | Study design/intervention | Sample/inclusion | Follow-up period | Primary outcome | Results |
|--------|---------------------------|------------------|------------------|----------------|---------|
| Physical activity | | | | | |
| Breast | | | | | |
| Chen et al (2011) | An evaluation of any associations of exercise after breast cancer diagnosis with total mortality and recurrence/disease-specific mortality after accounting for conditions that restrict exercise participation | 4826 women with stage I–III breast cancer identified 6 months after diagnosis through the population-based Shanghai Cancer Registry and recruited into the study between 2002 and 2006 | Median follow-up of 4.3 years | Exercise was assessed 6, 18 and 36 months after diagnosis | After adjustment for QoL, clinical prognostic factors and other covariates, exercise during the first 36 months after diagnosis was inversely associated with total mortality and recurrence/disease-specific mortality, with hazard ratios of 0.70 (95% confidence interval: 0.56 – 0.88) and 0.60 (95% CI: 0.47 – 0.76), respectively. Significant dose–response relationships between total and recurrence/disease-specific mortality rates and exercise duration and MET scores were observed (all P < 0.05). The exercise–mortality associations were not modified by menopausal status, comorbidity, QoL or body size, assessed ≥ 6 months after diagnosis. |
| Holick et al (2008) | Prospective cohort study examining the relationship between post-diagnosis recreational physical activity and risk of breast cancer death | Women with a history of invasive breast cancer, diagnosed between the ages of 20 and 79 years (n = 4482) | Maximum of 6 years post-diagnosis (median = 5.6 years post-diagnosis) | Mortality from breast cancer; mortality from any cause | Women who engaged in greater levels of activity had a significantly lower risk of dying from breast cancer (HR = 0.65; 95% CI = 0.59 – 0.76; P = 0.05) and 0.60 (95% CI = 0.47 – 0.76), respectively. Significant dose–response relationships between duration and MET scores were observed (all P < 0.05). |
| Holmes et al (2005) | Prospective observational study (Nurses’ Health Study) to determine whether physical activity among women with breast cancer decreases their risk of death from breast cancer | 2987 female registered nurses, diagnosed with stage I, II or III breast cancer | Women were diagnosed between 1984 and 1998 and followed until death or June 2002 | Breast cancer mortality risk | Compared with women who engaged in < 3 MET-h per week of physical activity, the adjusted relative risk (RR) of death from breast cancer was 0.80 (95% CI = 0.60 – 1.06) for 3 – 8.9 MET-h per week; 0.50 (95% CI = 0.31 – 0.82) for 9 – 14.9 MET-h per week; 0.45 (95% CI = 0.31 – 0.82) for 9 – 14.9 MET-h per week; and 0.60 (95% CI = 0.40 – 0.89) for ≥ 21.0 MET-h per week (P for trend = 0.05). |
| Ibrahim and Al-Homaidh (2011) | Meta-analysis of physical activity and survival after breast cancer diagnosis. A comprehensive literature search identified six studies. The search was limited to randomised, case–control, cohort or observational peer-reviewed clinical studies and reviews in English language | 2108 patients with breast cancer | N/A | Breast cancer survival | Pre-diagnosis PA reduced all-cause mortality by 18% but had no effect on breast cancer death. Post-diagnosis PA reduced breast cancer deaths by 34% (HR = 0.66, 95% CI = 0.57 – 0.77, P < 0.00001), all-cause mortality by 41% (HR = 0.59, 95% CI = 0.53 – 0.63, P < 0.00001) and disease recurrence by 24% (HR = 0.76, 95% CI = 0.66 – 0.87, P = 0.000001). Breast cancer mortality was reduced by pre-diagnosis PA in women with body mass index (BMI) ≥ 25 kg/m², whereas post-diagnosis PA reduced the risk among those with BMI ≥ 25 kg/m². On the other hand, post-diagnosis PA reduced all-cause mortality regardless of the BMI. The analysis showed that post-diagnosis PA reduced breast cancer deaths (HR = 0.50, 95% CI = 0.34 – 0.74, P = 0.00001) and all-cause mortality (HR = 0.64, 95% CI = 0.58 – 0.73, P = 0.00001) among patients with oestrogen receptor (ER)-positive tumour, whereas women with ER-negative disease showed no benefit. |
| Irwin et al (2008) | The Health, Eating, Activity, and Lifestyle Study (HEAL): Prospective observational study investigating the association between pre- and post-diagnosis physical activity and mortality among women with breast cancer | 933 women diagnosed with local or regional breast cancer | 5 – 8 years from diagnosis (median = 6 years) | Mortality from breast cancer; mortality from any cause | Compared with inactive women, the multivariable HRs for total deaths for women engaging in at least 9 MET-h per week were 0.49 (95% CI = 0.45 – 1.06, P = 0.045) for those active in the year before diagnosis and 0.33 (95% CI = 0.15 – 0.73, P = 0.046) for those active 2 years after diagnosis. Compared with women who were inactive both before and after diagnosis, women who increased physical activity after diagnosis had a 45% lower risk of death (HR = 0.55; 95% CI = 0.22 – 1.38), and women who decreased physical activity after diagnosis had a four-fold greater risk of death (HR = 3.9; 95% CI = 1.45 – 10.50). |
Irwin et al. (2009)
RCT – Post-menopausal breast cancer survivors were identified from the Yale-New Haven Hospital Tumour Registry and randomly assigned to an exercise (n = 37) or usual care (n = 38) group. The exercise group participated in 150 min per week of moderate-intensity aerobic exercise. The usual care group was instructed to maintain their current physical activity level.

Table 5 (Continued)

| Author | Study design/intervention | Sample/inclusion | Follow-up period | Primary outcome | Results |
|--------|---------------------------|------------------|-----------------|----------------|---------|
| Irwin et al. (2009) | RCT – Post-menopausal breast cancer survivors were identified from the Yale-New Haven Hospital Tumour Registry and randomly assigned to an exercise (n = 37) or usual care (n = 38) group. The exercise group participated in 150 min per week of moderate-intensity aerobic exercise. The usual care group was instructed to maintain their current physical activity level. | 75 post-menopausal breast cancer survivors | 6 months | A fasting blood sample was collected on each study participant at baseline and 6 months. Blood levels of insulin and IGF were measured with ELISA. | On average, exercisers increased aerobic exercise by 1.29 min per week compared with 0.45 min per week among usual-care participants (P < 0.001). Women randomised to exercise experienced decreases in insulin, IGF-I and IGFBP-3, whereas women randomised to usual care had increases in these hormones. Between-group differences in insulin, IGF-I and IGFBP-3 were 20.7% (P = 0.089), 89% (P = 0.026) and 7.9% (P = 0.006), respectively. |
| Ugboh et al. (2008, 2009) | RCT examining the impact of physical activity on insulin levels in participants randomly assigned to: (1) Physical activity intervention: a 16-week supervised strength training and home-based cardiovascular training protocol (two supervised 50-min strength training sessions per week and 90 min of home-based aerobic physical activity weekly); (2) Control group: routine care for 16 weeks. | 101 sedentary, overweight breast cancer survivors (stage I–III) who had completed chemotherapy and/or radiation therapy 3 months previously (mean age = 53 years) | On completion of the 16-week intervention | Fasting insulin and glucose levels | There were significant post-treatment decreases in insulin levels for the exercise group but not for the control group. Fasting insulin concentrations decreased by an average of 2.86 μU/ml in the exercise group (P = 0.03), with no significant change in the control group (decrease of 0.27 μU/ml, P = 0.63) (P = 0.07). |
| Patterson et al. (2010) | A review of the published epidemiological research on lifestyle and breast cancer outcomes. Research included RCTs, cohort studies or case–control studies of breast cancer outcomes. Included studies had been published in the previous 10 years (1999–2009), as well as a few large studies published > 10 years ago. Papers were included only if there were at least 500 participants. Studies of exposure biomarkers such as serum nutrient concentrations were not included, nor were studies with intermediate markers of breast cancer (e.g., mammographic density) or non-invasive lesions (e.g., ductal carcinoma in situ). | Breast cancer | Not reported | Additional breast cancer events and mortality | Four studies of physical activity and additional breast cancer outcomes were identified, two of which were not identified in the current search strategy (Friedenrich, 2009; Sternfeld, 2009). None of these studies found a statistically significant association, although there was a trend towards a protective effect; the weighted average was 0.86. Nine studies of physical activity and breast cancer mortality were identified, four of which were not identified through the current search strategy (Borugan et al. 2004; Dal Maso et al. 2008; Friedenrich, 2009; Sternfeld, 2009), of which three showed a statistically significant protective effect (Holmes et al. 2005; Holis et al. 2008; Irwin et al. 2008). The weighted average for the association of lifetime, at diagnosis or post-diagnosis physical activity with mortality was 0.71. |
| Pelzmei and Demark-Wahnefried (2011) | Literature review designed to synthesise recent progress in lifestyle interventions in light of current guidelines put forth by the ACS, WCRF/AICR, and ACSM. The PubMed database was searched for terms of cancer survivor(s) or neoplasms/survivor, cross-referenced with MeSH terms of lifestyle, health behaviour, physical activity, exercise, body weight, obesity, weight loss, diet, nutrition, psycho and/or lifestyle variables, whereas dietary interventions improve diet quality, nutrition-related biomarkers and body weight. | All cancer survivors, but primarily breast cancer | N/A | Fitness, strength, physical function and cancer-related psychosocial variables, whereas dietary interventions improve diet quality, nutrition-related biomarkers and body weight. | There has been an increase in the number and methodological rigour of the studies in this area, with 21 RCTs identified in the past 3 years. Results suggest that physical activity interventions are safe for cancer survivors and produce improvements in fitness, strength, physical function and cancer-related psychosocial variables, whereas dietary interventions improve diet quality, nutrition-related biomarkers and body weight. Preliminary evidence also suggests that diet and exercise may positively influence biomarkers associated with progressive disease and overall survival (e.g., insulin levels, oxidative DNA damage and tumour proliferation rates). |
| colorectal | Prospective, randomised trial exploring the impact of exercise on oxidative DNA damage. Patients were allocated to a moderate intensity (MI) exercise group following primary therapy, or to a high-intensity exercise group. | 48 colorectal cancer patients following primary therapy (mean age = 59 years) | Concentrations were determined immediately before and after completion of the exercise programme | Urinary 8-oxo-dG excretion concentration was determined by a highly sensitive detection method using highly sensitive detection method using high-performance liquid chromatography coupled to electrospray ionisation mass spectrometry (HPLC-ESI-MS). | M1 exercise significantly reduced urinary 8-oxo-dG excretion levels from 8.47 ± 1.99 to 5.81 ± 1.45 (ng mg⁻¹ creatinine, mean ± s.e., P = 0.02), whereas H1 exercise resulted in a non-significant increase from 5.00 ± 1.31 to 7.11 ± 1.63 (ng mg⁻¹ creatinine, P = 0.18). Clinical characteristics (gender, age, body mass index (BMI), diet, chemotherapy/radiation) were not associated/correlated with urinary 8-oxo-dG levels. |
| Author                  | Study design/intervention                                                                 | Sample/inclusion                  | Follow-up period       | Primary outcome                                                                 | Results                                                                                                                                 |
|-------------------------|-------------------------------------------------------------------------------------------|-----------------------------------|------------------------|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Haydon et al (2006)     | Melbourne Collaborative Cohort Study, examining colorectal cancer incidence against self-reported physical activity | 526 Australians with colorectal cancer | Median = 5.5 years     | Disease-specific survival                                                        | Exercisers had an improved disease-specific survival (HR = 0.73, 95% CI = 0.54 – 1.00). The benefit of exercise was largely confined to stage II – III tumours (HR = 0.49, 95% CI = 0.30 – 0.79). Increasing percentage body fat resulted in an increase in disease-specific deaths (HR = 1.33 per 10 kg, 95% CI = 1.04 – 1.71) |
| Meyerhardt et al (2005) | Prospective study of recreational physical activity and prognosis among stage III colon cancer patients enrolled in an RCT of post-operative adjuvant chemotherapy | 816 patients with stage III colon cancer | 6 months post-therapy  | Disease-free survival                                                           | Levels of physical activity were associated with significantly improved disease-free survival among patients with stage III colon cancer. The HR for DFS for individuals in the highest quintile (>25 MET-h per week) was 0.65 (95% CI = 0.38 – 1.11; P for trend = 0.02) compared with those in the lowest quintile of PA. This relationship varied by gender, with a HR = 0.33 (95% CI = 0.11 – 0.99) for women (P for trend = 0.046) and a HR = 0.89 (95% CI = 0.44 – 1.78) for men (P for trend = 0.3) |
| Prostate Bouke et al (2011) | Participants were randomised to a 12-week lifestyle programme comprising aerobic and resistance exercise, plus dietary advice or standard care | 50 (25 per group) advanced prostate cancer patients receiving androgen suppression therapy (AST) for a minimum of 6 months | Baseline, after the intervention and at 6 months | Exercise behaviour, dietary macronutrient intake, quality of life, fatigue, functional fitness and biomarkers associated with disease progression | The lifestyle group showed improvements in exercise behaviour (P < 0.001), dietary fat intake (P = 0.01), total energy intake (P = 0.005), fatigue (P = 0.002), aerobic exercise tolerance (P < 0.001) and muscle strength (P = 0.033) compared with standard care controls. No effects on clinical prostate cancer disease markers were observed |
| Kenfield (2010)         | Prospective study (Health Professionals Follow-up Study) assessing the relationship of physical activity, and duration and pace of walking, with total and prostate cancer-specific mortality | 2686 men with prostate cancer     | 4 years                | Prostate cancer mortality                                                       | Men who were physically active, especially those engaging in >3 MET-h of total activity, had a 35% lower risk of death from any cause (HR = 0.65; 95% CI = 0.52 – 0.82) and a modest non-significant reduction in risk of prostate cancer death (HR = 0.88; 95% CI = 0.52 – 1.49), after adjustment for other risk factors for PCA mortality and pre-diagnosis physical activity. Although no benefit from walking was observed for PCA mortality, men who walked >90 min per week vs those who walked <20 min per week had a 23% lower risk of all-cause mortality (95% CI = 0.61 – 0.97; P = 0.01). In addition, compared with men who walked <90 min at an easy walking pace, those who walked >90 min at a normal to very brisk pace had a 51% lower risk of all-cause mortality (95% CI = 0.37 – 0.64). More vigorous activity, and longer duration of activity, was associated with significant further reductions in risk for all-cause mortality. More vigorous activity was associated with a borderline-significant reduction in risk for PCA mortality |

Abbreviations: ACSM = American College of Sports Medicine; AICR = American Institute for Cancer Research; CI = confidence interval; DFS = disease-free survival; ELSA = enzyme-linked immunosorbent assay; FS = flaxseed-supplemented; HI = high intensity; HR = hazard ratio; IGFBP-3 = insulin-like growth factor-binding protein 3; IGF = insulin-like growth factor; LF = low-fat; MET = metabolic equivalent tasks; MI = moderate intensity; N/A = not available; PA = physical activity; PCa = prostate cancer; PSA = prostate-specific antigen; QoL = quality of life; RCT = randomised controlled trial; WCRF = World Cancer Research Fund.
There are some notable differences between the WINS and WHEL trials, both of which examined the efficacy of a low-dietary-fat diet on breast cancer prognosis. The main difference was that a better prognosis was found for WINS participants, which could be explained by the lack of weight loss in WHEL participants compared with WINS participants. It is possible that the potential mechanism of benefit produced from low-fat, high-fruit and vegetable (particularly carotenoids) diets may be through changes in weight. Indeed, the majority of studies in this review demonstrate an association between weight and cancer-related risks, with higher weight increasing the risks (Hebert et al. 1998; Enger et al., 2004; Lahmann et al., 2005; Patterson et al., 2010). Furthermore, a randomised prospective study by Elkort et al. (1981), reviewed by Bekkering et al. (2006), designed to evaluate the effects of long-term (12 months) enteral nutritional support in a group of breast cancer patients undergoing chemotherapy, suggests that any significant change in initial body weight, either a gain or a loss, is associated with an increased risk of recurrent disease. The WINS had a much higher rate of attrition by study completion, when compared with WHEL attrition rates. There was a completion rate of 39% vs 44% in the intervention and control groups, respectively, after 5 years of the WINS study. In comparison, the completion rate was 83% for the intervention group vs 89% for the control group, after 4 years of the WHEL study. Furthermore, although the level of fat reduction was similar between studies, other dietary behaviours were also targeted in the WHEL trial, including increased vegetable, fruit and fibre intake. This poses implications for determining the primary mechanism of benefit obtained from the intervention.

Expanding on the potential effect of carotenoids on cancer outcomes, higher intake of carotenoid-rich fruit and vegetables has been associated with a significant reduction in oxidative stress biomarkers, in relation to both DNA damage and lipid peroxidation (Giovannelli et al., 2002). Diets low in antioxidants, particularly antioxidant carotenoids provided as vegetables and fruit in the diet, may contribute to increased oxidative stress. However, in a subanalysis of a purposive sample of participants (n = 207), Thomson et al. (2007) found a significant inverse association between total plasma carotenoid concentrations and oxidative stress; dietary carotenoid levels were not significantly associated with oxidative stress indicators, although dietary lycopene and lutein/zeaxanthin were modestly associated with 8-OHdG levels (P = 0.054 and 0.088, respectively). Key findings include a significant inverse association between total plasma carotenoid concentrations and oxidative stress as measured by urinary 8-OHdG, and a moderately significant inverse association with 8-iso-PGF2α, a protective association that was not shown for dietary carotenoid intake. This is a small sample size, but they were taken from the WHEL RCT.

Additional dietary sources being investigated in terms of breast cancer progress and recurrence include soy and vitamin D. Boyapati et al. (2005) found soy intake pre-diagnosis to be unrelated to disease-free breast cancer survival (HR = 0.99; 95% CI = 0.73 – 1.33 for the highest tertile compared with the lowest tertile) (n = 1459). In a prospective cohort study, Goodwin et al. (2009) found that women (n = 512) with deficient vitamin D levels had a significantly increased risk of distant recurrence (HR = 1.94; 95% CI = 1.16 – 3.25) and death (HR = 1.73; 95% CI = 1.05 – 2.86) than did those with sufficient levels.

The review and meta-analysis by Patterson et al. (2010), of epidemiological research on physical activity, diet and adiposity, identified 41 relevant studies with primary outcomes of additional breast cancer events and mortality. A summary of the study focus and meta-analysis findings is as follows:

- For three studies examining carbohydrates (Holmes et al., 1999; Borugian et al., 2004; McEligot et al., 2006), findings were mixed with one report of a statistically significant protective effect (McEligot et al., 2006): the weighted average was 0.74.
- For five studies on dietary fat (Jain et al., 1994; Zhang et al., 1995; Borugian et al., 2004; McEligot et al., 2006; Dal Maso et al., 2008), four HRS showed a trend towards increased risk, although only one had a statistically significant finding (McEligot et al., 2006): the weighted HR was 1.53.
- For three studies of dietary fibre, there was a trend towards being protective (Holmes et al., 1999; Borugian et al., 2004; McEligot et al., 2006), with two being statistically significant (Holmes et al., 1999; McEligot et al., 2006): the weighted average was 0.63.
- Of four studies that reported on protein (Holmes et al., 1999; Borugian et al., 2004; McEligot et al., 2006; Dal Maso et al., 2008), two found a statistically significantly protective association (Holmes et al., 1999; Borugian et al., 2004): the weighted average was 0.72.
- A prudent dietary pattern (high intakes of fruits, vegetables, whole grains, legumes, poultry, and fish) appeared protective (Kronenke et al., 2005; Kwan et al., 2009), with one statistically significant finding (Kwan et al., 2009). In contrast, the Western dietary pattern (high intakes of refined grains, processed and red meats, desserts, high-fat dairy products, and fries) was associated with a non-significant increase in risk (Kronenke et al., 2005; Kwan et al., 2009).

An important strength of the review by Patterson et al. (2010) is that data are reported separately for observational studies vs RCTs. Furthermore, studies are included only if they comprise at least 500 participants. Unfortunately, however, they did not report on studies of exposure markers such as serum nutrient concentrations, which can offer insights into the protective benefit of dietary interventions.

The protective effect of fibre found in the systematic review by Patterson et al. (2010) was partially supported by a more recent observational study conducted by Belle et al. (2011). In this study, the HEAL (Health, Eating, Activity, and Lifestyle) study, an inverse association was found between fibre intake and breast cancer mortality (n = 688). Multivariate-adjusted hazard rate ratios (HRRs) comparing high with low intake were 0.53 (95% CI = 0.23 – 1.23) and 0.75 (95% CI = 0.43 – 1.31). A threshold effect was observed, whereby no additional benefit was observed for intakes of ≥ 9 g per day. Fibre intake was inversely associated with breast cancer-specific mortality (HRR = 0.68; 95% CI = 0.27 – 1.70) and risk of non-fatal recurrence or second occurrence (HRR = 0.68; 95% CI = 0.27 – 1.70), but results were not statistically

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**Figure 1** Flow of information.
significant. High-fibre diets are generally low in fat, which might be one mechanism of benefit. Another possible mechanism of benefit is that fibre-rich diets have been shown to improve insulin sensitivity, with an associated reduction in circulating oestrogen levels, which might suppress breast cancer growth.

**Colorectal cancer** Bekkering et al (2006) reported on six high-fibre diet interventions that showed little effect on the risk of recurrence. Data from one trial in patients with colorectal pre-invasive lesions evaluated the effect of calcium vs placebo on the risk of developing cancer and found little evidence of effect. On combining the data from two β-carotene trials, four multivitamin trials, and one trial containing a multivitamin group and an N-acetylcysteine (found in high-protein foods) group, there was weak evidence of a reduction in the risk of colorectal polyps (abnormal growth of tissues in the colon) with these two. Two calcium interventions showed some evidence of a reduced risk of recurrence.

One prospective observational study was identified in the current review. Meyerhardt et al (2007) examined dietary patterns in patients (n = 1009) who had been successfully treated for stage III colorectal cancer, following them for a median of 5.3 years. During this time, there was a significant difference between those who had followed a ‘prudent’ diet (i.e., high intake of fruit, vegetables, poultry, and fish) and those who had followed a ‘Western’ diet (i.e., high intake of meat, fat, refined grains, sweets, and desserts). A higher intake of a Western dietary pattern was associated with a significantly worse disease-free survival (DFS). Compared with patients in the lowest quintile of the Western dietary pattern, those in the highest quintile experienced an adjusted HR (AHR) for DFS of 3.25 (95% CI = 2.04–5.19; P for trend <0.001). The Western dietary pattern was associated with a similar detriment in recurrence-free survival (AHR = 2.85; 95% CI = 1.75–4.63) and OS (AHR = 2.32; 95% CI = 1.36–3.96), comparing the highest with the lowest quintiles (both with P for trend <0.001). The reduction in DFS with a Western dietary pattern was not significantly modified by sex, age, nodal stage, body mass index, physical activity level, baseline performance status or treatment group. In contrast, the prudent dietary pattern was not significantly associated with cancer recurrence or mortality.

**Prostate cancer** Bekkering et al (2006) did not provide any evidence for the role of diet in prostate cancer survival.

A recent prospective, randomised intervention by Aronson et al (2010) examined a 4-week low-fat diet compared with a Western diet in newly diagnosed prostate cancer patients (n = 18). Findings suggest that a low-fat diet might inhibit the growth rate of hormonally responsive prostate cancer cells. A more recent exploration of changes in 50 plasma cytokines and angiogenic factors (CAFs) in prostate cancer patients enrolled in this RCT suggests that a low-fat diet without flaxseed may reduce levels of specific inflammatory CAFs and suggests that the NF-κB pathway may be a mediator of these changes (Heymach et al, 2011).

Richman et al (2010) used telephone to promote increased consumption of fruit and vegetables over a 6-month study period (n = 43). Although men in the intervention group consumed significantly more vegetables and had significantly higher serum levels of carotenoids, as confirmed by increases in serum carotenoids, the intervention produced a non-significant increase in PSA; there was a non-significant change in mean PSA levels, of +2.28 in the intervention group vs −0.06 in the control group (P = 0.29). This was a small-scale study reliant on self-report for broadly defined dietary changes.

Richman et al (2010) conducted a prospective study of the association between post-diagnostic consumption of processed and unprocessed red meat, fish, poultry and eggs and the risk of prostate cancer recurrence or progression (n = 1294). They found that intakes of processed and unprocessed red meat, fish, total poultry and skinless poultry were not associated with recurrence or progression. Greater consumption of eggs and poultry with skin was associated with twofold increases in risk in a comparison of extreme quantiles: eggs (HR = 2.02; 95% CI = 1.10–3.72; P for trend = 0.05) and poultry with skin (HR = 2.26; 95% CI = 1.36–3.76; P for trend = 0.003). The overall findings suggest that the consumption of processed or unprocessed red meat, fish or skinless poultry post diagnosis may not be associated with prostate cancer recurrence or progression, whereas post-diagnosis consumption of eggs and poultry with the skin may increase the risk.

A recent review conducted by Hori et al (2011) highlights that there is some evidence suggesting that green tea, isoflavone, lycopene, cruciferous vegetable and omega-3 polyunsaturated fatty acid intake is beneficial in the prevention and/or progression of prostate cancer. They also found evidence to suggest that a high total fat, meat (especially well cooked) and multivitamin intake may be associated with an increased risk of developing prostate cancer, but more research is required to establish its effect on progression. In Hori et al’s (2011) review, RCTs were favoured over observational studies, indicating quality data synthesis.

**Dietary supplements**

The systematic review on the effects of nutritional and physical activity interventions and cancer survival by Bekkering et al (2006) reports there to be little evidence that a dietary supplement taken separately or in combination with a healthy diet or physical activity is associated with a reduction in all-cause mortality. Of nine trials that included an antioxidant supplement, no evidence was found for an association between this intervention and all-cause mortality, compared with placebo or usual treatment. There was no evidence of an effect of retinol (vitamin A) on all-cause mortality, cancer mortality or DFS compared with the usual treatment.

Table 4 presents evidence obtained on dietary supplements for breast, colorectal and prostate cancers.

**Breast cancer** In a case–control study testing whether antioxidant supplements reduce breast cancer recurrence or mortality (n = 385), Fleischauer et al (2003) found that antioxidant supplement users compared with non-users were less likely to have a breast cancer recurrence or breast cancer-related mortality (OR = 0.54, 95% CI = 0.27–1.04). Vitamin E supplements showed a modest protective effect when used for > 3 years (OR = 0.33, 95% CI = 0.10–1.07). Furthermore, risks of recurrence and disease-related mortality were reduced among women using vitamin C and E supplements for > 3 years. However, these findings are all statistically non-significant, with widespread CI levels, and there is no information regarding which factors would indicate the dietary patterns of these two groups and which may confound the findings of the study.

In a systematic review of published epidemiological studies on lifestyle and breast cancer mortality, Patterson et al (2010) found that in four studies (Jain et al, 1994; Holmes et al, 1999; McEligot et al, 2006; Dal Maso et al, 2008), there was an overall trend towards being protective. Statistically significant protective associations were found for higher intakes of calcium (Holmes et al, 1999), vitamin C (Jain et al, 1994) and vegetables (McEligot et al, 2006). A notable weakness in the review by Patterson et al (2010) is that included studies were limited to those vitamins and minerals that can be obtained through self-report and therefore physiological markers of supplement intake were not evaluated. Furthermore, given the heterogeneity across studies, it is impossible to provide conclusive recommendations for these supplements.
Colorectal cancer The WCRF report provides evidence that serum albumin, alkaline phosphatase, lactate dehydrogenase levels and percentage targeted caloric intake are significant independent predictors of survival duration (Evans et al., 1987). On the other hand, there was no evidence that either β-carotene or vitamins C and E reduced the incidence of colorectal adenomas (Greenberg et al., 1994). Vitamin C therapy also showed no advantage over placebo therapy with regard to either the interval between the beginning of treatment and disease progression or patient survival (Moertel et al., 1985). The evidence within the current review adds very little to these findings.

Ng et al (2008) examined pre-diagnosis levels of vitamin D in a cohort of participants with colorectal cancer (n = 304) from the Nurses’ Health Study, which demonstrated that higher plasma (blood) vitamin D levels were associated with a significant reduction in overall mortality. The focus of the study was on pre-diagnosis vitamin D. The findings suggested a 48% reduction between the highest and lowest quartiles of plasma 25(OH)D. However, for colorectal cancer mortality, the multivariate HR was attenuated to a statistically non-significant reduction of 39% between the extreme quartiles. Ulrich and Holmes (2008) pointed out that this study needs to be followed up with a larger cohort and an RCT to determine whether colorectal cancer survivors should be advised to take vitamin D supplements.

Ng et al (2010) also conducted a prospective, observational study exploring the influence of multivitamin supplements on cancer recurrence and death after a curative resection of colorectal cancer (n = 1038). Compared with non-users, the multivariate HR for DFS was 0.94 (95% CI = 0.77 – 1.15) for patients who used multivitamins. Similarly, multivitamin use during adjuvant chemotherapy was not significantly associated with recurrence-free survival (multivariate HR = 0.93; 95% CI = 0.75 – 1.15) or OS (multivariate HR = 0.92; 95% CI = 0.74 – 1.16). This is believed to be the first study to examine the impact of multivitamin use on survival in colorectal cancer patients. Furthermore, the sample size was reasonably large and the fact that participants were from a clinical trial reduced the impact of heterogeneity by disease stage. However, this study did rely on self-reports of multivitamin use, which poses issues around accuracy and reliability, as does the fact that multivitamin users are also likely to partake in other health behaviours that might impact the outcomes, including ‘healthy’ dietary patterns.

Prostate cancer Ornish et al (2005) used an RCT to investigate the effects of intensive dietary and lifestyle changes on PSA levels of men with early prostate cancer (n = 93). The lifestyle changes in this study included a low-fat, vegan diet supplemented with soy, vitamin E, fish oils, selenium and vitamin C, together with a moderate physical activity programme, and stress management techniques such as yoga. It was found that PSA levels decreased by 4% at 12 months in the intervention group, but increased by 6% in the control group. Furthermore, the growth of LNCaP prostate cancer cells was inhibited almost 8 times more by serum in the intervention group compared with the control group (70% vs 0.9%). Changes in serum PSA and diet in the intervention group were significantly associated with the degree of change in diet and lifestyle. However, the intervention also included a physical activity element, leading to lack of clarity as to whether it was the dietary changes, physical activity or a combination of both that may affect PSA levels. In addition, the intensity of this intervention and associated behavioural changes might not be easily translated into normal healthy eating patterns (White et al., 2009).

Bettuzzi et al (2006), in a year-long clinical trial, have demonstrated that daily consumption of green tea can produce a 10-fold decrease in the rate at which prostate intraepithelial neoplasia (a pre-cancerous condition) progresses to prostate cancer. Support for these findings is offered by researchers of the Louisiana State University, who conducted an uncontrolled, open-label, single-arm phase II clinical trial testing the efficacy of Polyphenol E, which contains the polyphenol antioxidants found in green tea (Mclarty et al., 2009). On taking 4 capsules of Polyphenol E daily (equivalent to 12 cups of green tea) for an average of 34.5 days leading up to radical prostatectomy, participants (n = 26) experienced significant reductions in the biomarkers used to monitor the likelihood of metastasis. Some patients demonstrated reductions >30%. Future research in this area would require a controlled trial to avoid the bias of an observational study with small sample size.

Salicylate intake has been implicated in the aetiology of prostate cancer, but Thomas et al (2009) have evaluated their influence on established cancer progression. In a randomised, double-blind, phase II study involving men (n = 110) with progressive prostate cancer who were counselled to eat less saturated fat and processed food, more fruit, vegetables and legumes, engage in physical activity more regularly and to stop smoking, men were then randomised to take sodium salicylate alone or combined with vitamin C, copper and manganese gluconates daily. Although there was no difference in outcome between those who received sodium salicylate alone or combined, the intervention as a whole (i.e., dietary counselling) slowed or stopped the rate of PSA progression from baseline to 40 patients (36.4%) for >1 year, and a further 10 patients were stabilised for 10 months. These data suggest that changes in dietary components towards a more healthy diet may potentially delay PSA progression, although further study on the effects of micronutrients is required.

The potential benefits of pomegranate juice on prostate cancer outcomes appear frequently in the media, and strong evidence of its efficacy can be found within the academic literature. In a phase II, open-label, single-arm clinical trial, men (n = 46) with recurrent prostate cancer who had increasing PSA after surgery or radiotherapy were treated daily with 8 oz (227 g) equivalent of pomegranate juice (Pantuck et al., 2006). Mean PSA doubling time significantly increased with treatment from 15 to 54 months, demonstrating a good indication of a relationship between the consumption of pomegranate juice and prostate health.

In a phase II trial testing the comparative effects of flaxseed supplementation (30 g per day) with and without a low-fat diet against controls who continued their usual diet, dietary fat restriction was not associated as strongly with prostate cancer cell growth as flaxseed supplementation (n = 161) (Demark-Wahnefried et al., 2008).

More recently, Epstein et al (2011) conducted a Swedish population-based cohort study examining whether dietary zinc assessed near the time of prostate cancer diagnosis was associated with improved disease-specific survival (n = 525). High dietary zinc intake was associated with a reduced risk of prostate cancer-specific mortality (P = 0.05). The association was stronger in men with localised tumours (HR = 0.24; 95% CI = 0.09 – 0.66; P for trend = 0.005).

Physical activity

Although rest is important in recovery from cancer treatment, there has traditionally been an overemphasis on conserving energy. An implication of this is that insufficient physical activity over time leads to loss of physical conditioning and muscular strength, which makes it difficult to perform even basic activities of daily living (Ness et al., 2006). There is substantial evidence that physical activity can help relieve treatment-related symptoms, such as fatigue (Stevinson and Courneya, 2009). However, there are now also promising data suggesting that physical activity after diagnosis is associated with improved survival. The precise mechanisms through which physical activity may influence cancer recurrence and mortality have not been established, but areas of ongoing research include the role of adiposity, metabolic and sex.
hormones, growth factors, immunological processes and chronic inflammation (Pekmezci and Demark-Wahnefried, 2011).

Guidelines have been published by the American College of Sports Medicine for patients with cancer (ACSM, 2010), which are compatible with the American Cancer Society's recommendation of 30–60 min of moderate-to-vigorous intensity physical activity at least 5 days per week for survivors who are otherwise healthy. There are currently no formal physical activity guidelines for cancer survivors in the United Kingdom. However, a recent expert statement by the British Association of Sports and Exercise Sciences on exercise and cancer survivorship (Campbell et al, 2011, Table 1) also recommends that unless otherwise advised, cancer survivors should follow the health-related physical activity guidelines produced in 2011 for the general UK population (Table 1). All cancer survivors, including those with existing disease or those who are undergoing difficult treatments, should be encouraged, as a minimum, to avoid being sedentary (Campbell et al, 2011).

Table 5 presents evidence on physical activity for breast, colorectal and prostate cancers.

Breast cancer  The systematic review carried out for the WCRF (Bekkering et al, 2006) on lifestyle and cancer survivorship focused on RCTs. A majority of those RCTs reviewed had quality of life as the primary outcome. None focused on all-cause mortality, whereas one study focused on cancer recurrence (Nieman et al, 1995). Nieman et al (1995) investigated the impact of 60 min of supervised weight training and aerobic activity 3 times each week for 8 weeks, and found that it did not significantly alter natural killer cell activity relative to the non-exercise control group and would potentially not reduce the risk of recurrence. Although the updated evidence review by Patterson et al (2010) found that there were more studies examining the impact of lifestyle factors on surrogate/biological markers of survival, there were still few studies testing the effects of lifestyle factors (diet and physical activity) on disease progression and OS.

The studies identified in the current review suggest that physical activity may mediate breast cancer recurrence through its effect on hormones, specifically by reducing the levels of oestrogen in the body (Friedenreich et al, 2010) or by shifting the metabolism of oestrogen to favour production of 2-hydroxyestrone (2-OHE) as opposed to 16α-hydroxyestrone (16α-OHE), the former of which has much weaker oestrogenic activity. This shift might also be the result of a change in lean body mass resulting from physical exercise (Campbell et al, 2007).

In a prospective observational study, Irwin et al (2008) compared with inactive women, the multivariable HRs for total mortality for women engaged in at least 9 MET hours (MET-h) per week (e.g., 2–3 h of brisk walking) were 0.69 (95% CI = 0.45–1.06; P = 0.045) for those active in the year before diagnosis and 0.33 (95% CI = 0.15–0.73; P = 0.046) for those active 2 years after diagnosis. Compared with women who were inactive both before and after diagnosis, women who increased their physical activity after diagnosis had a 45% lower risk of death (HR = 0.54; 95% CI = 0.32–0.91) after adjusting for baseline physical activity after diagnosis had a fourfold greater risk of mortality (HR = 3.95; 95% CI = 1.45–10.50). Consistent with this, a larger prospective observational study of breast cancer survivors  (n = 4482) showed that women who engaged in greater levels of activity had a significantly lower risk of breast cancer mortality (HR = 0.65; 95% CI = 0.39–1.08 for 2.8–7.9 MET-h per week; HR = 0.59; 95% CI = 0.35–1.01 for 8.0–20.9 MET-h per week; and HR = 0.51; 95% CI = 0.29–0.89 for ≥210 MET-h per week; P < 0.05) (Holick et al, 2008). Overall, women who were physically active for ≥2.8 MET-h per week (e.g., walking at an average pace of 2–2.9 mph for 1 h) had a significantly lower risk of mortality from breast cancer (35–49% reduction) (Holick et al, 2008). The reduced risk of mortality was limited to total or moderate-intensity physical activity; no benefit was noted for vigorous-intensity activity.

Ligibel et al (2008) conducted an RCT to test the impact of weight training on insulin levels in overweight, sedentary stage I–III breast cancer survivors (n = 101). The rationale for this study is that the beneficial effects of physical activity on cancer survival might be mediated through beneficial changes in metabolic hormones (insulin), insulin-like growth factor (IGF)-1 and its binding protein IGFBP-3 (Pekmezci and Demark-Wahnefried, 2011). Women were randomly assigned to one of two conditions: a 16-week supervised strength training and home-based cardiovascular training protocol (two supervised 30-min strength training sessions per week and 90 min of home-based aerobic physical activity weekly) or a control group (routine care for 16 weeks before being offered consultation with a physical activity trainer at the end of the control period). Participation in the intervention was associated with a significant decrease in insulin levels. Therefore, the relationship between physical activity and breast cancer recurrence may be mediated, in part, through changes in insulin levels. Indeed, in an RCT examining the relationship of IGF-1 levels with an increased risk of breast cancer mortality, it was found that women randomised to the exercise group (150 min per week of moderate-intensity aerobic exercise) experienced decreases in insulin, IGF-1 and IGFBP-3, whereas women randomised to usual care (maintaining current physical activity) had increases in these hormones (Irwin et al, 2009). Between-group differences in insulin, IGF-1 and IGFBP-3 were 20.7% (P = 0.026), 8.9% (P = 0.76) and 17.9% (P = 0.006), respectively. The authors infer that exercise-induced decreases in IGF may mediate the observed association between higher levels of physical activity and improved survival in women diagnosed with breast cancer.

In a systematic review by Patterson et al (2010), leisure-time physical activity (i.e., sports/recreational) was associated with a 30% decreased risk of mortality. The association between physical activity before and after diagnosis and breast cancer survival has been further examined in a meta-analysis conducted by Ibrahim and Al-Homaibd (2011). This meta-analysis of six studies, although limited in size, demonstrated some promising findings. In particular, it was found that post-diagnosis physical activity reduced breast cancer deaths by 34% (HR = 0.66; 95% CI = 0.57–0.77, P = 0.0001), all-cause mortality by 41% (HR = 0.59; 95% CI = 0.53–0.65, P = 0.0001) and disease recurrence by 24% (HR = 0.76; 95% CI = 0.66–0.87; P = 0.0001). The results are an encouraging contribution to the growing evidence for the beneficial effect of physical activity on breast cancer outcomes.

A recent population-based study using the Shanghai Cancer Registry examined the association between physical activity after diagnosis with recurrence and total and cancer-specific mortality in women with stage I–III breast cancer (n = 4826) (Chen et al, 2011). The findings indicate that physical activity during the first 36 months after diagnosis was inversely associated with total mortality and recurrence/disease-specific mortality, with HRs of 0.70 (95% CI = 0.56–0.88) and 0.60 (95% CI = 0.47–0.76), respectively. Significant dose–response relationships between total and recurrence/disease-specific mortality rates and exercise duration and MET scores were also observed (P < 0.05). Associations between physical activity and mortality were not modified by menopausal status, comorbidity or body size, which was assessed ~6 months after diagnosis.

Colorectal cancer  The observational study by Haydon et al (2006) demonstrated that self-reported leisure-time physical activity (at least once per week) before diagnosis was associated with improved cancer-specific survival in colorectal cancer survivors (n = 526). Those who reported regular physical activity (at least once per week) before diagnosis had improved cancer-specific survival (73% 5-year survival) compared with those not reporting...
regular physical activity (61% 5-year survival). However, this study does suffer from the methodological limitations of an observational design. Another prospective study of stage III colorectal cancer survivors (n = 816), over a 3-year period after surgery and chemotherapy, showed increases in DFS and OS with increasing volumes of physical activity (P < 0.05) (Meyerhardt et al, 2005).

One mechanism by which physical activity may exert its influence on colorectal cancer prognosis could be through the modulation of oxidative DNA damage, which is implicated in carcinogenesis and may be important for cancer progression and relapse. In a hospital-based exercise programme comparing moderate vs high-intensity exercise over 2 weeks for 30–40 min per day, colorectal cancer patients (n = 48) showed reduced oxidative DNA damage as measured by pre- and post-intervention urinary 8-oxo-dG excretion concentrations (8.47 ± 1.99 to 5.91 ± 1.45 ng ml⁻¹ creatinine, P = 0.02) (Allgayer et al, 2008). On the other hand, high-intensity exercise was associated with increased DNA damage (5.00 ± 1.31 to 7.11 ± 1.63 ng ml⁻¹ creatinine, P = 0.18) (Allgayer et al, 2008). This suggests that the intensity of physical activity might have an important role in colorectal cancer progression, raising the need for RCTs to further examine this.

Another potential mechanism of benefit is reduced weight in colorectal cancer survivors who are physically active. Drawing on seven RCTs, Sinicrope et al (2010) provide evidence for BMI being significantly associated with both DFS and OS. There is also some evidence of gender differences; being overweight was associated with improved OS in men, whereas being underweight was associated with significantly worse OS in women.

Prostate cancer The underlying mechanisms for the direct anti-cancer effect of lifestyle has been indicated in a study that took serum (blood plasma) from men undergoing a low-fat, high-fibre diet and physical activity intervention, and added it to androgen-dependent LNCaP cells in the laboratory (Soliman et al, 2009). There was decreased growth and increased apoptosis (cell death), associated with a reduction in serum IGF-1. These findings suggest that diet and physical activity interventions might slow prostate cancer progression and aid in its treatment during the early stages of development.

In a prospective study, Kenfield (2010) examined the data of 2686 men from the Health Professionals Follow-Up Study and found that men who engaged in >3 MET-h of weekly physical activity after diagnosis reduced their risk of death by 35% compared with men who engaged in fewer than 3 MET-h of weekly activity. Furthermore, men who walked 90 min per week at a normal-to-brisk pace had a 51% lower risk of death due to any cause compared with men who walked ≤90 min at an easy pace. To reduce their risk of cancer-specific death, men had to engage in vigorous activity, such as jogging (6 MET-h). A sensitivity analysis in which updating of activity was stopped before a diagnosis of metastasis showed that the results remained unchanged. Self-report of exercise is a limiting factor in the design of this study. However, the findings are indicative of a protective gradient in benefit of physical activity intensity levels in terms of prostate cancer/overall mortality, which is in contrast with the breast cancer study conducted by Holick et al (2008), which found no increased benefit of partaking in vigorous activity.

In a more recent RCT, Bourke et al (2011) examined the association between exercise and prostate cancer outcomes (n = 50). Patients receiving androgen suppression therapy for a minimum of 6 months were randomised to a 12-week lifestyle programme comprising aerobic and resistance exercise, plus dietary advice (n = 25) or standard care (n = 25). Although the lifestyle group showed improvements in exercise behaviour (P < 0.001), dietary fat intake (P = 0.001), total energy intake (P = 0.005), fatigue (P = 0.002), aerobic exercise tolerance (P < 0.001) and muscle strength (P = 0.033) compared with the standard-care control group, no effects on clinical prostate cancer disease markers were observed. This was a very small study that cannot be generalised to other prostate cancer survivors. Furthermore, its primary aim was to examine outcomes such as QoL and fatigue, and therefore the design lacked a focus on measuring markers of disease progression. A larger study is required, with refined outcomes.

DISCUSSION

The purpose of this review was to update the literature review undertaken in 2010 for the NCSI (Davies et al, 2010), which covered evidence on lifestyle and cancer survivorship between 2006 and 2010, and to include observational studies that were in the main excluded from the WCRF survivorship systematic review (Bekkering et al, 2006). By updating the 2010 review and refining the focus to the lifestyle factors of diet, physical activity and supplements in relation to breast, prostate and colorectal cancer survivorship, further insight has been gained into how these factors might affect cancer prognosis.

The early contradictory findings from the large-scale WINS and WHEL trials in the 1990s and their subsequent secondary analysis studies (Khodadkar et al, 2003; Chlebowski et al, 2006, 2008; Pierce et al, 2007; Thomson et al, 2007; Dwyer et al, 2008; Gold et al, 2009; Caan et al, 2011) established a strong focus on the role of fat reduction and significant changes in diet (including fat reduction) as important factors for breast cancer prognosis. This was especially so for post-menopausal breast cancer survivors. A recent review and meta-analysis by Patterson et al (2010) of the findings of the WINS and WHEL trials and the secondary analysis studies does indicate that, even after accounting for study weaknesses, dietary intervention without weight loss or physical activity is not sufficient to improve breast cancer prognosis. A study by Ewertz et al (2011) indicates that obesity is an independent prognostic risk factor for the development of distant metastases and mortality after breast cancer diagnosis (Sinicrope and Dannenberg, 2011). Although at this point strong and definitive evidence that weight loss in obese patients (BMI > 30 kg m⁻²) with breast cancer will improve cancer outcomes is lacking, weight reduction and increased physical activity may well achieve the objective and should also have a positive effect on comorbid conditions such as diabetes and cardiovascular disease.

The findings for colorectal and prostate cancer are limited. The 2006 review by Bekkering et al failed to find supporting evidence for a protective effect of dietary fibre on the risk of recurrence for colorectal cancer. The study by Meyerhardt et al (2007) does indicate that a healthy diet may be associated with better outcomes on recurrence and mortality. In particular, a high Western diet (i.e., high intakes of meat, fat, refined grains and dessert) was associated with worse DFS compared with a prudent diet (i.e., high intakes of fruits and vegetables, poultry, and fish). The mechanism of benefit remains unclear as a prudent diet was not independently associated with disease-free survival. Therefore, differences in weight as opposed to diet might be the most plausible explanation for the effect of a Western diet on prognosis.

More recent research focuses on the effect of obesity on the colorectal outcomes of DFS and OS (Sinicrope et al, 2010). The findings of this well-designed study extend the effect of obesity beyond its association with colon cancer risk, to demonstrate that obesity is an independent prognostic variable in colon cancer survivors, which shows differences by gender. Further research will need to study the impact of interventions for obesity on colorectal cancer survivors.

For prostate cancer, an RCT by Ornish et al (2005) found that PSA levels decreased by 4% at 12 months in prostate cancer patients consuming a vegan diet supplemented with soy,

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vitamin E, fish oils, selenium and vitamin C, together with a moderate physical activity programme and stress management techniques. In contrast, PSA levels increased by 6% in the control group. Furthermore, the growth of LNCaP prostate cancer cells was inhibited almost 8 times more by serum from the diet group compared with the control group. Both changes in serum PSA and LNCAP cell growth were significantly associated with the degree of change in diet and lifestyle, suggesting that dietary changes can be effective in prostate cancer outcomes.

Clinical trials have also examined the potential benefits of various supplements for prostate cancer outcomes, with weak beneficial effects from pomegranate juice (Pantuck et al, 2006), flaxseed (Demark-Wahnefried et al, 2008), zinc (Epstein et al, 2011) and salicylate intake (Thomas et al, 2009). For pomegranate juice, the mean PSA doubling time significantly increased from 15 to 54 months, indicating a relationship between the consumption of pomegranate juice and prostate health. For flaxseed, the authors report that dietary fat restriction was not associated as strongly with prostate cancer cell growth as flaxseed supplementation (Demark-Wahnefried et al, 2008). On the other hand, high dietary zinc intake was associated with a reduced risk of prostate cancer-specific mortality, the association being stronger in men with localised tumours (Epstein et al, 2011). For salicylate supplementation, although there was no difference in outcome between those who received sodium salicylate and those who did not, the data suggest that changes in dietary components towards a more healthy diet may potentially delay PSA progression (Thomas et al, 2009). These studies offer promising findings, but all comprised a small sample size, ranging from 46 to 525 participants. These findings are synthesised in the review by Hori et al (2011), which also found green tea, isoflavone, lycopene, cruciferous vegetable and omega-3 polyunsaturated fatty acid intake to be beneficial in the prevention and/or progression of prostate cancer.

In evaluating the impact of diet and physical activity on cancer progression and survival, evidence from prospective observational studies suggests that physical activity and diet may be associated with improved cancer progression and recurrence (Khaodhier et al, 2003; Holmes et al, 2005; Chlebowski et al, 2006, 2008; Pierce et al, 2007; Thomson et al, 2007; Dwyer et al, 2008; Holick et al, 2008; Irwin et al, 2008, 2009; Gold et al, 2009; Goodwin et al, 2009; Belle et al, 2011; Caan et al, 2011; Chen et al, 2011). In particular, the evidence suggests that a low-fat, high-fibre diet might be protective against breast, colorectal and prostate cancer recurrence and progression. There is, however, a paucity of evidence for dietary supplements. Furthermore, any findings from observational studies need to be interpreted with caution because of issues of systematic and random error in self-reported data (Patterson et al, 2010). This is why, as done by Patterson et al (2010), findings from observational studies need to be evaluated against findings from the more rigorous WHEL and WINS RCTs, which produced no sufficient benefit for breast cancer outcomes. It is, however, possible that these RCTs did not target the most relevant dietary components, nor did they adequately distinguish different dietary changes.

Reduced adiposity may be achieved through a low-fat, high-fibre diet and regular physical activity. However, questions remain about the degree of weight loss that may improve the outcomes of cancer survivorship. More rigorous research, particularly RCTs, is required to further distinguish the specific dietary factors and supplements involved in cancer outcomes. On the other hand, evidence from prospective studies suggests that regular physical activity is associated with improved cancer prognosis for breast, prostate and colon cancer survivors (Meyerhardt et al, 2005; Haydon et al, 2006; Allgayer et al, 2008; Irwin et al, 2008, 2009; Ligibel et al, 2008, 2011; Kenfield, 2010; Patterson et al, 2010; Pekmezi and Demark-Wahnefried, 2011) and, indeed, a dose response for increased physical activity and better outcomes (Chen et al, 2011). More vigorous activity, and longer duration of activity, has also been associated with significant further reductions in the risk for all-cause mortality (Kenfield, 2010). RCTs have shown physical activity to cause changes in the biomarkers of cancer risk, whereas observational studies have shed some light on the benefit from physical activity for cancer outcomes (McTiernan, 2008). Overall, the evidence suggests that the physical activity recommendations of the Department of Health (2011) are sufficient for cancer survivors – a total of at least 30 min a day of moderate-intensity physical activity on ≥ 5 days of the week. Even when this might seem too much, survivors can be reminded that the minimum 30 min per week can be tailored to individual needs and capabilities through graded or progressive physical activity. The evidence for breast cancer further suggests that for survival benefits to be achieved from physical activity, no less than moderate-to-vigorous activity is required (Holick et al, 2008). A recent literature review conducted by Szymlek-Gay et al (2011) suggests that although physical activity levels are low among cancer survivors, most people are interested in increasing their participation. The review also highlights that preferences and adherence to physical activity programmes differ across a range of demographic, medical and behavioural variables, suggesting the importance of tailoring exercise programmes to patient- and disease-specific needs.

Some notable limitations within the current review are that there are less published data for recurrence and cancer events than for all-cause and cancer-specific mortality. Furthermore, some of the studies comprise small sample sizes and few offer evidence for the long-term effects of diet and physical activity on cancer prognosis. Some of the studies that do offer convincing evidence for the beneficial health outcomes associated with diet and physical activity interventions tend to lack external validity. Nevertheless, incomplete scientific evidence can still inform reasonable conclusions that can guide lifestyle choices for cancer survivors (Doyle et al, 2006).

CONCLUSIONS

The evidence within this review builds upon that in other reviews and suggests that excess weight is an important risk factor for cancer prognosis, which is modifiable through diet and physical activity. However, important questions still remain regarding the degree of weight loss, and levels and intensity of physical activity required to reduce cancer outcomes. As weight gain and a sedentary lifestyle are common after a cancer diagnosis, there is a clear need to target the achievement and maintenance of a healthy weight in cancer survivors. One of the most efficacious ways to achieve this is through dietary changes and the uptake of an active lifestyle, both of which place responsibility and control into the hands of the cancer survivor. The NCSI highlights that people living with or beyond cancer would like to have a more active role in their health care. They want to know how to look after themselves after a cancer diagnosis, including what diet and lifestyle changes they should make, so they can return to a ‘normal’ life as much as possible (Macmillan Cancer Support, 2008). The challenge, therefore, is in integrating lifestyle support into standardised models of aftercare for cancer survivors.

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