REVIEW

A systematic review of the effect of diet in prostate cancer prevention and treatment

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Introduction

Prostate cancer (PC) is the third most commonly diagnosed cancer in men, and the sixth most commonly diagnosed cancer overall (American Institute for Cancer Research & World Cancer Research Fund (AICR & WCRF), 2007). PC is the malignant growth of prostate gland cells. Epidemiological research has shown that ethnic background, age, genetics and particularly environmental factors, such as diet, influence the risk of PC. In Caucasian Americans, the incidence is approximately 200-fold greater than in Chinese men, whereas the incidence in Afro-Americans is approximately 300-fold greater than that in Chinese men (Parkin et al., 1999). Those with a first degree relative with PC have a three-fold increased risk; indicating a gene–environment interaction (Gann, 2002). However, studies in migrant populations point to a strong influence of environmental factors on the risk of PC. In migrants to the USA from Japan and China, the rate of PC was found to increase compared to those in their native countries and, by the second generation, the incidence rate was already approaching that of average Americans (Staszewski & Haenszel, 1965; Tomiaga, 1985; Shimizu et al., 1991). A recent study conducted in south asians in the USA, UK, Singapore and India confirms an increased incidence of PC in migrants, and concluded that diet may be a contributing factor (Rastogi et al., 2008).

We provide an evidence-based review of dietary recommendations for the prevention and treatment of PC. The aim is to review dietary recommendations for the prevention and treatment of PC. Evidence is provided for the following areas: (1) dietary factors proposed to decrease the risk of PC; (2) dietary factors proposed to increase the risk of PC; and (3) dietary intervention post-diagnosis.

Search methods

The literature search was conducted through Medline Ovid, Pubmed and Cochrane Collaboration library. Key words were: diet, nutrition, PC and specific dietary therapy.
elements (Table 1). Article references were searched further for additional relevant publications. Articles were searched from January 1965 until April 2008. Publications were only included if they were level of evidence IIIb or greater (Table 2) (Phillips et al., 2001). To limit the size of the review and, consequently, the number of references, meta-analyses and review articles were cited in place of the original publications. The identified studies were

### Table 1  Search strategy

<table>
<thead>
<tr>
<th>Database</th>
<th>Time span</th>
<th>Search strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane library</td>
<td>2008</td>
<td>Prostate Cancer, Prostate; and diet and nutrition and supplements Cancer and Nutrition and/or diet</td>
</tr>
<tr>
<td>Medline</td>
<td>1996–2008</td>
<td>Prostate Cancer, Prostate; and diet and nutrition and supplements Prostate Cancer and Individual nutritional items and supplements*</td>
</tr>
<tr>
<td>EMBASE</td>
<td>1985–2008</td>
<td>Prostate Cancer, Prostate; and diet and nutrition and supplements</td>
</tr>
<tr>
<td>PubMed</td>
<td>–2008</td>
<td>Prostate Cancer, Prostate; and diet and nutrition and supplements</td>
</tr>
</tbody>
</table>

*Individual nutritional items and supplements refer to those mentioned in the review.

### Table 2  Evaluation of evidence on the impact of dietary components in preventing prostate cancer

<table>
<thead>
<tr>
<th>Food component</th>
<th>Conclusion from review of the evidence</th>
<th>Level of evidence/recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomato and lycopene</td>
<td>Decrease risk</td>
<td>Ila B</td>
<td>More than two servings tomato sauce week(^{-1}) or 5 mg day(^{-1}) lycopene; cooked appears to be more effective than raw</td>
</tr>
<tr>
<td>Selenium</td>
<td>Decrease risk</td>
<td>Ila B</td>
<td>Low selenium level with increased risk. Selenium supplement may reduce risk – 50–200 (\mu g) day(^{-1}) in people with low serum selenium</td>
</tr>
<tr>
<td>Vitamins E(\alpha)-tocopherol</td>
<td>Decrease risk</td>
<td>Iib C</td>
<td>Increased risk of other disease with high-dose intake</td>
</tr>
<tr>
<td>Cruciferous vegetables</td>
<td>Decrease risk</td>
<td>Iib C</td>
<td>Possible role in reducing risk of prostate cancer; more than five servings a week</td>
</tr>
<tr>
<td>Soy/isoflavones</td>
<td>Decrease risk</td>
<td>Iib C</td>
<td>In some studies soy consumption was low.</td>
</tr>
<tr>
<td>Fish and omega-3 fatty acids</td>
<td>No clear benefit</td>
<td>Iib C</td>
<td>Genetic polymorphisms may affect results</td>
</tr>
<tr>
<td>Folate</td>
<td>No association</td>
<td>Iib D</td>
<td>Too few studies</td>
</tr>
<tr>
<td>Green tea</td>
<td>No association</td>
<td>Iib D</td>
<td>Too few studies</td>
</tr>
<tr>
<td>Alcohol/wine</td>
<td>No association</td>
<td>Iib D</td>
<td>Too few studies</td>
</tr>
<tr>
<td>Meat</td>
<td>Increase risk</td>
<td>Iib C</td>
<td>Grilled or processed meats, more than five servings a week</td>
</tr>
<tr>
<td>Calcium</td>
<td>Increase risk</td>
<td>Iib B</td>
<td>Increased risk with high calcium intake (&gt; 1.5 g day(^{-1}))</td>
</tr>
<tr>
<td>Dairy</td>
<td>Increase risk</td>
<td>Iib C</td>
<td>Include skim or low fat</td>
</tr>
<tr>
<td>Fat</td>
<td>Increase risk</td>
<td>Iib C</td>
<td>Particularly high intake of animal and saturated fats</td>
</tr>
<tr>
<td>(\beta)-Carotene</td>
<td>Increase risk</td>
<td>Iib D</td>
<td>Increased risk of other diseases with high dose intake (&gt; 20–30 mg day(^{-1})), particularly smokers</td>
</tr>
</tbody>
</table>

Level of evidence (based on Oxford Centre for Evidence-Based Medicine Levels of Evidence, May 2001)

<table>
<thead>
<tr>
<th>Level</th>
<th>Therapy/prevention, aetiology/harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iia</td>
<td>Systematic review (with homogeneity) of cohort studies</td>
</tr>
<tr>
<td>Iib</td>
<td>Individual cohort study (including low quality RCT, e.g. &lt; 80% follow-up)</td>
</tr>
<tr>
<td>Iic</td>
<td>‘Outcomes’ Research; Ecological studies</td>
</tr>
<tr>
<td>Iila</td>
<td>'Systematic review (with homogeneity) of case-control studies</td>
</tr>
<tr>
<td>IIIb</td>
<td>Individual case-control study</td>
</tr>
</tbody>
</table>

Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Consistent level 1 studies</td>
</tr>
<tr>
<td>B</td>
<td>Consistent level 2 or 3 studies or extrapolations from level 1 studies</td>
</tr>
<tr>
<td>C</td>
<td>Level 4 studies or extrapolations from level 2 or 3 studies</td>
</tr>
<tr>
<td>D</td>
<td>Level 5 evidence or troublingly inconsistent or inconclusive studies of any level</td>
</tr>
</tbody>
</table>
assessed and scored according to evidence-based guidelines defined by the Oxford Centre for Evidence-Based Medicine (Phillips et al., 2001).

The authors acknowledge that a comprehensive monograph on diet and cancer prevention by the World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) was published in 2007 (AICR & WCRF, 2007). However, the present review includes an assessment of dietary intervention post-diagnosis, and some dietary factors not mentioned in the previous report, such as cruciferous vegetables, fish/omega-3 fatty acids, green tea and alcohol, on the prevention of PC.

**Dietary factors proposed to decrease risk of prostate cancer**

Plant-based food constituents; including micronutrients (e.g. vitamins C and E) and phytochemicals (e.g. carotenoids, flavonoids, phyto-oestrogens and isothiocyanates) have been shown to possess certain anti-carcinogenic properties (Kirsh et al., 2007). Carotenoids, found mainly in yellow/orange vegetables/fruits and cruciferous vegetables, are proposed to retard cancer-cell development, and inhibit tumour promotion (Steinmetz & Potter, 1991). Some flavonoids have antioxidant properties (Steinmetz & Potter, 1991), leading to the binding of free radicals, and the reduction of oxidative damage of DNA and possibly cancer (Sies, 1997). Isothiocyanates suppress the expression of neoplasia in previously initiated cells (Wattenberg et al., 1985). This section focuses on the epidemiological evidence for individual groups of dietary items postulated to specifically reduce the risk of PC. Evidence-based recommendations on these dietary factors are presented in Table 2.

**Tomato and lycopene**

Lycopene is a carotenoid, mainly found in tomatoes and watermelon, which is proposed to limit oxidative damage to cellular macromolecules. In *vitro*, lycopene impacts on insulin-like growth factor 1 (IGF-1) signalling, where high IGF-1 levels have been correlated with an increased susceptibility to PC (Santillo & Lowe, 2006).

Lycopene consumption was inversely associated with the occurrence of PC in case–control studies (Gann et al., 1999; Jian et al., 2005) and tomato intake and serum lycopene levels were linked with a reduced incidence of advanced PC, or the progression of PC in three recent case–control studies (Darlington et al., 2007; Giovannucci et al., 2007; Peters et al., 2007). Beneficial associations were observed for tomato or vegetable juices and ketchup in one study (Darlington et al., 2007). Two large cohort studies have, however, shown that tomato products and lycopene do not appear to prevent the incidence of PC (Kirsh et al., 2006; Peters et al., 2007).

A meta-analysis of 11 case–control and ten cohort studies found an association between lycopene intake and a decreased risk of PC (Etminan et al., 2004). The AICR/WCRF expert panel also came to the conclusion that evidence suggests that tomato/lycopene most likely has a protective effect against PC, based on both cohort and case–control studies (AICR & WCRF, 2007). In summary, the evidence available to date suggests that a high versus low intake of foods containing lycopene decreases the risk of PC, where cooked produce may be more potent than raw products.

**Cruciferous vegetables (CV)**

Cruciferous vegetables (CV), or Brassica vegetables, are part of the Brassicaceae family; and include cauliflower, brussels sprouts, bok choy and broccoli. Glucosinolates compounds found in CVs have been shown to protect cells from DNA damage, induce apoptosis, and inhibit cell proliferation of PC (Kirsh et al., 2007). CVs also have a high content of other phytochemicals, such as phenethyl isothiocyanate, sulforaphane and indole-3-carbinol, which have been shown to exhibit potential anti-cancer properties (Stoner et al., 1997; Ashok et al., 2001, 2002; Zhang et al., 2003; Singh et al., 2005).

An inverse association between CVs and the incidence of PC has been found in several case–control studies (Jain et al., 1999; Cohen et al., 2000; Kolonel et al., 2000; Joseph et al., 2004) and two cohort studies (Schuurman et al., 1999; Kirsh et al., 2007). By contrast, four cohort studies have concluded that CVs are not cancer preventative (Hsing et al., 1990; Giovannucci et al., 2003; Key et al., 2004; Stram et al., 2006). Overall, there is no convincing data indicating that the consumption of CVs reduces the incidence of PC. However, for those under the age of 65 years, CV consumption was inversely associated with PC (Giovannucci et al., 2003). Kirsh et al. (2007) similarly found that a high intake of CVs decreased the risk of disseminated PC compared to a low intake (*P* = 0.02); providing some evidence for the possible reduction of risk of advanced PC with dietary intervention. Large randomised controlled trials could provide more definitive evidence.

**Green tea**

Polyphenolic compounds are found in green tea. Some of these compounds have been found to prevent metastases of PC, and induce apoptosis and cell growth inhibition (Santillo & Lowe, 2006). A study of the combined inhibitory effects of green tea polyphenols and selective
cyclooxygenase-2 inhibitors performed both in vitro and in vivo found that tumour growth inhibition was enhanced, leading to lower prostate-specific antigen levels, and lower IGF-I levels (Adhami et al., 2007). A large prospective cohort study in Japan found that green tea was not associated with localised PC, but was found to be associated with a dose-dependent decrease in the risk of advanced PC for men drinking more than 5 cups a day (Kurahashi et al., 2008). Further investigations are warranted.

Soy

Isoflavones, especially genistein and daidzein, are mainly found in soybeans. Genistein inhibits enzymes associated with the transmission of signals from cellular growth factor receptors, which are expressed at high levels in transformed cells (Messina & Messina, 1991). Isoflavonoids obtained from soy have been shown to inhibit the growth of both benign and malignant prostate epithelial cells in vitro (Hedlund et al., 2006). A study of soy protein isolate consumption in 58 men demonstrated an effect on androgen receptor expression, which suggests that soy consumption could be beneficial in preventing PC (Hamilton-Reeves et al., 2007). This hypothesis is supported by a retrospective epidemiological study, and two prospective studies that concluded that soy intake was correlated with reduced risk (Hebert et al., 1998; Jacobsen et al., 1998; Nagata et al., 2007). According to the WCRF/AICR report, the findings of seven cohort studies, 11 case–control studies and eight epidemiological studies were inconsistent, but provided limited evidence on the effectiveness of soy (AICR & WCRF, 2007). A possible confounding factor may relate to low soy intakes in participants in some studies, as well as the difficulties involved in extrapolating from Asian studies to other population groups.

Oily fish and long-chain n3 polyunsaturated fatty acids

Long-chain n3 polyunsaturated fatty acids (LCPUFA) are commonly found in oily fish. Evidence reviewed by Santillo and Lowe (2006) has shown that LCPUFA inhibit cell growth and serum prostate-specific antigen (PSA) protein expression. Cyclo-oxygenase-1 (COX-1) and COX-2 have both been found to be increased in human PC, indicating that they may play a role in the formation of PC (Kirschchenbaum et al., 2000). Furthermore, COX-2 expression has been found to be modulated by omega-3/omega-6 polyunsaturated ratios (Aronson et al., 2001), suggesting a possible effect of dietary fish oils in the prevention of PC. This association is reportedly caused by a genetic variation in the COX-2 gene, meaning that only carriers of this genetic variant had a decreased risk of PC with respect to the consumption of LCPUFA (Hedelin et al., 2007). One epidemiological study found a negligible reduction in risk of PC (7%) in men who consumed fish three times a week versus two times a week (Augustsson et al., 2003). In two small cohort studies of flaxseed, which is a source of LCPUFA and phyto-oestrogens, the results obtained suggested that flaxseed combined with dietary fat restriction has an effect on the biology of PC and associated markers (Demark-Wahnefried et al., 2001, 2004). Finally, a review of eight prospective cohort studies and nine case–control studies did not provide sufficient evidence to demonstrate that the intake of fish and marine fatty acids reduced the risk of PC (Terry et al., 2003).

Vitamin E

Vitamin E may aid in cancer prevention due to its role as an intracellular antioxidant (Steinmetz & Potter, 1991). It functions as an antiprostaglandin; whereby prostaglandins are believed to have a role in PC (Santillo & Lowe, 2006). Side effects can occur with over consumption of vitamins and minerals (Santillo & Lowe, 2006).

Vitamin E intake was associated with deceased risk of PC in three case–control and one cohort study (Vlajinac et al., 1997; Chan et al., 1999; Deneo-Pellegrini et al., 1999; Tzonou et al., 1999). In a large cohort study (VITAL), a higher intake of vitamin E reduced the risk of advanced PC (Peters et al., 2008). However, no effect was noted for vitamin E intake in four cohort (Hartman et al., 1998; Rodriguez et al., 2004; Weinstein et al., 2007; Wright et al., 2007) and three case–control studies (Hayes et al., 1988; Hsing et al., 1990; Nomura et al., 1997). The WCRF/AICR expert panel examined a total of six cohort studies, 14 case–control studies and one ecological study regarding dietary/serum vitamin E, and concluded that there is a ‘probable’ association between vitamin E intake and a decreased risk of PC (AICR & WCRF, 2007). One note of caution is that a vitamin E consumption of over 400 IU was found to increase all-cause mortality (Miller et al., 2005). These data suggest that vitamin E supplementation may decrease the risk of PC, particularly in smokers and in those with low serum levels; however, high vitamin E intakes (≥ 400 IU) may prove to be harmful.

Selenium

Selenium has been shown to induce apoptosis, inhibit cellular proliferation and inhibit angiogenesis (Chan et al., 2005). Reductions in the incidence of PC have been reported by up to 50–65% with high versus low selenium levels (Chan et al., 2005). However, no reduction in risk was found with long-term intake of > 50 μg of selenium.
per day (Peters et al., 2008). A meta-analysis of 20 epidemiological studies showed a significant increase in the incidence of PC in men with low selenium levels (Brinkman et al., 2006). The findings of these observational studies are supported by one randomised interventional trial of cancer prevention, where the primary end point was nonmelanoma skin cancer, showing an approximately 50% reduced risk of PC with a daily 200 μg selenium supplement, particularly in men with low selenium levels (Clark et al., 1996; 1998; Duffield-Lillico et al., 2003). In summary, selenium intake probably reduces the risk of PC, particularly in men with low serum selenium levels.

Energy balance and weight loss

Obesity has been correlated with advanced PC or aggressive disease (Demark-Wahnefried & Moyad, 2007). Obesity has been reported to contribute to almost 14% of all cancer deaths in men (Greenwald, 2004). The data also suggest that a higher body mass index is associated with more aggressive or progressive diseases, and a worse outcome (Freedland, 2005; Giovannucci et al., 2007). It has long been demonstrated that serum testosterone levels and lipid levels can be reduced with a low-fat diet (Hamalainen et al., 1983; Rosenthal et al., 1985). The results of one case–control study suggest that there was no association between PC incidence and nonenergy effects of total fat and monounsaturated fat intake (Rohan et al., 1995). However, one cohort study demonstrated an inverse association between the intake of monounsaturated fat and the risk of death from PC (Kim et al., 2000). Another large cohort study also found that men who lose weight may reduce their risk of PC (Rodriguez et al., 2007). Thus, excessive energy intake and obesity, independent of dietary fat consumption, may increase the risk of PC.

Dietary factors postulated to increase the risk of prostate cancer

This section focuses on the clinical studies on specific groups of dietary factors proposed to increase the risk of PC. Evidence-based recommendations on these dietary factors are presented in Table 2.

Meat

Meat cooked at high temperatures can produce carcinogens such as 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) (Felton et al., 1986). Exposure to PhIP has been shown to induce PC in rats (Shirai et al., 1997). Clinical studies, however, are inconclusive (Norrish et al., 1999; Cross et al., 2005; Tang et al., 2007).

In a review of more than 20 studies, six cohort studies demonstrated an increased risk, and two cohort studies reported a decreased risk, of PC (Kolonel, 2001). One cohort study of 51 529 men reported an increased risk of metastatic PC with red meat (Michaud et al., 2001). However, two other cohort studies found no significant association between the intake of total meat and the incidence of PC (Park et al., 2007a; Rohrmann et al., 2007).

Of five studies conducted to examine the relationship between processed meat intake and PC, four found an increased risk of PC (Veierod et al., 1997; Schuurman et al., 1999; Michaud et al., 2001); however, one of these reports was not statistically significant (Rohrmann et al., 2007). Altogether, studies on meat consumption point to a possible increased risk of PC with high meat consumption, especially processed or charcoaled meats.

Dairy products

Dairy products have been proposed to cause PC through a number of factors, including lactose and calcium. In a meta-analysis of 16 prospective trials, dairy products were found to slightly increase the risk of PC (relative risk (RR) = 1.09; 95% confidence interval (CI) = 1.00–1.2) (Gao et al., 2005; Severi et al., 2006). Furthermore, Qin et al. (2007) performed a meta-analysis on 18 cohort studies and concluded that there was an increased risk of PC associated with dairy foods (RR = 1.13; 95% CI = 1.02–1.24). Subsequent to the publication of these meta-analyses, several large cohort studies have been published. Three of these five studies found no strong evidence for the positive association between dairy products and PC (Park et al., 2007b; Torniainen et al., 2007; Van Der Pols et al., 2007). Of these studies, a 65-year follow-up found an inverse association between dairy intake and PC (Van Der Pols et al., 2007). Another recent cohort study found a decrease in the risk of advanced PC in smokers with high dairy consumption (Neuhausser et al., 2007). By contrast, the ATBC Cancer Prevention Study reported that calcium or some related component contained in dairy products may be associated with an increased risk of PC (Mitrou et al., 2007). A US cohort study (CLUE II) found that a higher intake of dairy products was positively associated with PC, but calcium intake was not (Rohrmann et al., 2007). The risk of PC is not confined to normal milk because some reports on the risk of PC include low-fat milk (Torniainen et al., 2007) or skimmed milk (Park et al., 2007b).

Calcium

The same meta-analysis reported by Gao et al. (2005) found that a high calcium intake was associated with an
increased risk of PC (RR = 1.32) (Gao et al., 2005; Severi et al., 2006). This is further supported by a more recent cohort study that also reported a positive association with calcium intake of > 1000 mg day\(^{-1}\) (Giovannucci et al., 2007). An intervention study of colorectal adenoma prevention found no increase in the risk of PC with an intake of up to 1.2 g calcium day\(^{-1}\) (Baron et al., 2005). This result is supported by the findings of the CLUE II study (Rohrmann et al., 2007) and the NIH-AARP Diet and Healthy Study (Park et al., 2007b). These data suggest that calcium, and possibly many other dietary factors, have a therapeutic range above which the benefit ceases and the risk for PC increases. Current data suggest that the ceiling for this range is approximately 1000 mg daily of calcium supplement.

\(\beta\)-carotene

\(\beta\)-carotene is a carotenoid that is converted to vitamin A in the gut. High-dose \(\beta\)-carotene intake leads to an increase in the risk of lung cancer and all-cause mortality in smokers (Goodman et al., 2004). Interestingly, in three cohort studies, no increase in risk of PC was noted with \(\leq 25\) mg day\(^{-1}\) (Rohan et al., 1995; Hennekens et al., 1996; Cook et al., 1999) and there was even a decrease in risk for those with low plasma lycopene levels (Hennekens et al., 1996). Consumption over 20 mg day\(^{-1}\) (only 40 mg/2 days) resulted in an increased risk of PC in one study (Heinonen et al., 1998). \(\beta\)-carotene was also associated with an increased risk of aggressive PC (Peters et al., 2007). A high \(\beta\)-carotene intake may increase the risk of PC; however, the evidence is limited. We concur with the WCRF/AICR report that \(\beta\)-carotene is ‘unlikely to have a substantial effect on the risk of PC’ (AICR & WCRF, 2007).

Fats

Intake of fats, such as saturated fats, has been reported to increase the risk of PC or advanced PC, with a few studies reporting the association (West et al., 1991; Bairati et al., 1998). Most studies examining the relationship between fat and PC are case-control studies. Based on current data, the strongest evidence suggests a positive association between total fats and animal fats, and an increased risk of PC, as shown in Table 3.

Dietary intervention post-diagnosis

This section reviews the existing evidence of diet modifications on PC post-diagnosis. There are fewer observational and interventional studies on the effect of diet and nutritional supplements on the progression of the disease after diagnosis compared to that reported for the prevention of PC. In this section of the review, only interventional studies were analysed. A number of limitations exist in many of these studies, such as small sample sizes, total energy intakes not being considered, the use of surrogate survival benefit end points using biochemical/cellular markers, no survival end point, many studies being nonrandomised, and some studies using a combination of different dietary and lifestyle-related factors so that interpretation of the effectiveness of individual factors is difficult. The lack of homogeneity in the stages of PC and treatment were other confounding factors. Serum PSA was used as the primary marker of tumour progression in many of these studies; however, the accuracy of PSA as the key indicator of tumour status and thus as a primary surrogate end point of survival is debatable (Van Weerden & Schroder, 2008). In spite of the above limitations, the available data provide some tantalising evidence for the effectiveness of dietary intervention in patients diagnosed with PC. Large, long-term randomised controlled trials will provide more definitive answers on this issue.

A total of five studies were defined by the authors to be plant-based (high fruit, vegetable and fibre diet) interventional studies (Saxe et al., 2001, 2006; Tymchuk et al., 2001, 2002; Shike et al., 2002; Ornish et al., 2005; Nguyen et al., 2006). These studies did not include supplements in the diet. Often, the studies were combined with exercise programmes or stress reduction techniques/counseling. Four of these studies noted a significant impact of dietary adjustment on PC progression, as measured by serum PSA or serum tumour inhibitory effect. One found no effect of dietary adjustment on PSA levels (Shike et al., 2002). In conclusion, the evidence suggests that dietary adjustment based on a plant-based diet including exercise and reduced fat consumption is possibly effective in

<table>
<thead>
<tr>
<th>Fat Type</th>
<th>Positive association for increased risk</th>
<th>No association or decreased risk</th>
<th>Increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat</td>
<td>20 (total studies)</td>
<td>6 (1 cohort)</td>
<td>Suggestive</td>
</tr>
<tr>
<td></td>
<td>(3 cohort)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animal or saturated fats</td>
<td>14 (3 cohort)</td>
<td>5 (2 cohort)</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Monounsaturated</td>
<td>8 (3 cohort)</td>
<td>4 (1 cohort)</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Polyunsaturated</td>
<td>6 (2 cohort)</td>
<td>5 (2 cohort)</td>
<td>No conclusion</td>
</tr>
<tr>
<td>(\alpha)-Linoleic</td>
<td>5 (2 cohort)</td>
<td>2 (1 cohort)</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Eicosapentaenoic acid</td>
<td>2</td>
<td>3 (1 cohort)</td>
<td>No conclusion</td>
</tr>
</tbody>
</table>

*As defined by food, nutrition, physical activity and the prevention of cancer: a global perspective: a project of World Cancer Research Fund International, 2007 (AICR & WCRF, 2007).*
Reducing PC progression; however, further studies are required.

Concerning lycopene intake, three studies showed significant decreases in serum PSA levels. In two studies investigating the effects of the daily consumption of 30 mg of lycopene, plasma IGF-1 levels and tumour size were decreased compared to control in one study (Kucuk et al., 2002) and leukocyte oxidative DNA damage and tissue oxidative damage were significantly reduced in the other study (Chen et al., 2001). A study by Jatoi et al. (2007) using a different study end point found that lycopene did not lead to a greater than 50% reduction in serum PSA levels.

One serum-based randomised placebo-controlled study found no association between PC and the intake of vitamins C and E (Hoenjet et al., 2005). In another interventional study, combined selenium, vitamin E and soy isoflavonoid supplementation reduced serum PSA levels (Joniau et al., 2007).

In a 6-year follow up of a large randomised controlled trial; smokers supplemented with vitamin E or β-carotene demonstrated a 32% decrease in the incidence of PC in those taking α-tocopherol, and a 23% increase in those taking β-carotene. The incidence of PC was decreased by 16% in those taking both supplements (Heinonen et al., 1998).

Two of five interventional studies that used soy supplementation showed a decrease in serum PSA marker of tumour progression in response to soy supplementation (Urban et al., 2001; Jarred et al., 2002; Hussain et al., 2003; Dalais et al., 2004; Devere White et al., 2004), and another study demonstrated an increase in tumour cell death (apoptosis), although there was no change in PSA levels (Jarred et al., 2002). In four randomised control trials with soy and a combination of other supplements (including vitamin E, selenium and lycopene), a statistically significant beneficial effect on serum PSA was demonstrated (Spentzos et al., 2003; Kranse et al., 2005; Ornish et al., 2005; Schröder et al., 2005). The dose of the soy supplement in these studies was in the range 20–900 mg day⁻¹.

In the two studies where a low-fat diet was combined with flaxseed, one demonstrated a significant reduction in PSA levels and benign prostatic epithelial proliferation rate (Demark-Wahnefried et al., 2004). In the other study, no difference in PSA levels was found; however, serum androgen levels were decreased (Demark-Wahnefried et al., 2001). In one study of a low-fat diet plus LCPUFA supplement, there was a significant increase in the LCPUFA/omega-6 fatty acids ratios in plasma and adipose tissue and, by implication, this could potentially reduce the progression of PC (Aronson et al., 2001).

The evidence-based recommendations for these dietary interventions in PC patients are summarised in Table 4.

### Conclusion

At present, there is no definitive evidence supporting a specific dietary therapy for reducing the risk of PC. The results of numerous studies, although not conclusive, suggest that general dietary modification has a beneficial effect on the prevention of PC. Care must be taken to ensure that over consumption of dietary supplements

<table>
<thead>
<tr>
<th>Table 4 Evaluation of evidence regarding dietary intervention post-diagnosis</th>
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<tbody>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td>Plant-based</td>
</tr>
<tr>
<td>Lycopene/tomato</td>
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<tr>
<td>Vitamin E</td>
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<tr>
<td>α-Tocopherol and β-carotene</td>
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<tr>
<td>Soy/isoﬂavones</td>
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<tr>
<td>Diet with soy and other supplements</td>
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<tr>
<td>Low-fat</td>
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</tbody>
</table>

*Evidence is based on serum and/or biological markers. PSA, prostate-specific antigen.
does not occur because it may be harmful (Lawson et al., 2007). Based on current data, the recommended diet for the prevention and management of PC comprises a diet low in fat, high in vegetables and fruits, and avoiding high energy intake, excessive meat, and high dairy products and calcium. In patients with PC, dietary therapy allows patients to be an active participant in their treatment; however care must be taken to ensure that the patient fully understands the minimal effect of current diet therapy with respect to the control of PC, and the risk of forgoing proven conventional treatments.

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