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Development of a Nutrition Guidebook for Men with Prostate Cancer to Reduce Treatment Morbidity and Comorbidity and Lower the Risk of Cancer Progression

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Background

Men diagnosed with prostate cancer may experience a host of cancer and treatment-related side effects that may be prevented and treated by lifestyle interventions including diet, body weight management and physical activity. In men with prostate cancer, lifestyle interventions have demonstrated the potential to reduce morbidity associated with treatment and reduce the risk of prostate cancer progression. Specifically, diet and exercise interventions are effective and non-invasive in negating weight gain and loss of muscle mass and bone mass resulting from long-term hormone therapy, with additional benefits to men in reducing common co-morbidities. Early evidence using biomarkers of disease progression suggests lifestyle interventions can reduce prostate cancer recurrence, and in men who are overweight or who gain weight there is also the potential to improve treatment outcomes. Currently however there are few evidence-based resources that address lifestyle interventions for this target population. Therefore the development of a guidebook on diet, energy balance and physical activity was undertaken by a multidisciplinary team to improve reliable nutrition education resources available to men with prostate cancer.

Purpose

To describe the development and implementation of a novel evidence-based nutrition education resource for prostate cancer survivors.

Methods

In preparation for the guidebook development a comprehensive review of scientific literature was undertaken by a multidisciplinary group (Van Patten, de Boer, Tomlinson Guns) as part of a team building grant from the Michael Smith Foundation for Health Research. The review uniquely prioritized evidence from randomized controlled clinical trials enrolling men with prostate cancer, that used either a surrogate biomarker of prostate cancer recurrence (such as Prostate-specific antigen [PSA] or PSA doubling time [PSAdt]) or where possible survival endpoints. This review was peer-reviewed and published as a manuscript in 2008 in The Journal of Urology (see Selected Reference). Along with other key references the scientific evidence was later translated into lay language and this formed the basis of the content for the nutrition education resource for men living with prostate cancer. The information was formatted as a guidebook and subsequently pilot-tested in men with prostate cancer from a local support group and reviewed by content experts, oncologists and clinicians. Various revisions and enhancements were made to the content of the guidebook and a second shorter resource (summary version) was also developed based on feedback from men with prostate cancer who sought a quick-reference guide.

Review Articles

Diet and Dietary Supplement Intervention Trials for the Prevention of Prostate Cancer Recurrence: A Review of the Randomized Controlled Trial Evidence

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Purpose: We review the effect of diet and dietary supplement interventions on prostate cancer progression, recurrence and survival.
Materials and Methods: A literature search was conducted in MEDLINE®, EMBASE® and CINAHL® to identify diet and dietary supplement intervention studies in men with prostate cancer using prostate specific antigen or prostate specific antigen doubling time as a surrogate serum biomarker of prostate cancer recurrence and/or survival.
Results: Of the 32 studies identified 9 (28%) were randomized controlled trials and the focus of this review. In these studies men had confirmed prostate cancer and elevated or increasing prostate specific antigen. Only 1 trial included men with metastatic disease. When body mass index was reported, men were overweight or obese. A significant decrease in prostate specific antigen was observed in some studies using a low fat vegan diet, soy beverage or lycopene supplement. While not often reported as an end point, a significant increase in prostate specific antigen doubling time was observed in a study on lycopene supplementation. In only 1 randomized controlled trial in men undergoing orchiectomy was a survival end point of fewer deaths with lycopene supplementation reported.
Conclusions: A limited number of randomized controlled trials were identified in which diet and dietary supplement interventions appeared to slow disease progression in men with prostate cancer, although results vary. Studies were limited by reliance on the surrogate biomarker prostate specific antigen, sample size and study duration. Well designed trials are warranted to expand knowledge, replicate findings and further assess the impact of diet and dietary supplement interventions on recurrence and treatment associated morbidities.

Key Words: diet, dietary supplements, prostatic neoplasms, recurrence

In North America prostate cancer is the most common cancer in men. There are 22,300 men diagnosed annually in Canada[1] and 186,295 estimated in 2008 in the United States, representing 25% of all cancers in men.[2] Approximately 1 in 8 men will be diagnosed in their lifetime while 1 in 27 will die of the disease.[1] The prostate cancer survival rate is high[2] and it is often curable by surgery or radiotherapy when confined to the gland. However, approximately 25% to 40% of patients may have recurrence within 5 years.[3] The high incidence of prostate cancer coupled with a long latency period affords a particularly attractive target for dietary and lifestyle interventions, especially since conventional treatments are often associated with considerable morbidity such as urinary or bowel dysfunction, impotence, fatigue, weight gain, muscle loss and osteoporosis.[4]

There is a large variation in prostate cancer rates worldwide[5] and migration studies show that cancer rates increase in men who immigrate to the United States,[6,7] suggesting an important role of environmental factors including diet in primary prevention. Environmental factors have also been speculated to be important in prostate cancer progression. The rationale and role of diet and dietary supplements in delaying or preventing prostate cancer progression and/or recurrence are well documented in recent reviews that have examined an increasing body of evidence from preclinical and epidemiological studies, and clinical trials.[8–11] Furthermore, data on diet related factors such as obesity show a strong association with prostate cancer and worse overall outcomes.[12] This early evidence suggests that nontoxic dietary, lifestyle and/or naturally derived interventions could potentially decrease the risk of prostate cancer recurrence and improve survival as well as reduce significant treatment associated morbidity and ameliorate many of the common side effects.

Prior reviews of diet (including body weight), dietary supplements and prostate cancer have focused primarily on evidence from in vitro, in vivo and epidemiological studies with limited use of RCTs.[8–12] Therefore, we provide a comprehensive evaluation of diet and dietary supplement inter-

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Editor's Note: **This article is the first of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 2724 and 2725.**

TABLE 1. *Summary of PSA end points for RCTs*

References	Intervention	Subjects and Design	PSA Findings and Significance
		Diet trials	
Dalais et al[16]	Phytoestrogen-rich diet: Soy grits (50 gm) or soy grits (50 gm) plus flaxseed (20 gm), wheat control Soy grits contain 117 mg isoflavones	Men with prostate Ca awaiting prostatectomy (26):* soy (8), soy and flaxseed (10), wheat (8); randomized, placebo controlled double blind clinical trial; intervention: 22–27 days; followup: none	PSA: statistically significant difference in % change between soy and placebo (−12.7% vs 40%; p = 0.02) based on a decrease from 7.16 ± 3.23 to 6.34 ± 3.05 ng/ml for soy compared to an increase from 5.81 ± 3.70 to 7.11 ± 4.23 ng/ml in control; statistical analysis of flaxseed compared to control not reported PSADT: not available
Kumar et al[17]	Phytoestrogen-rich diet: Soy protein beverage (60 gm protein‡ and 60 mg genistein)	Men with prostate Ca on watchful waiting (59): soy (29), placebo (30); randomized, placebo controlled double blind clinical trial; intervention: 12 wks; followup: none	PSA: no difference in mean change in total PSA between soy and placebo based on 7.38 ± 5.62 to 6.77 ± 4.96 ng/ml for soy and 7.45 ± 5.36 to 6.89 ± 5.47 ng/ml for placebo (p = 0.96) or free PSA (p = 0.13) PSADT: not available
Bylund et al[15]	Phytoestrogen-rich diet: Rye bran bread (295 gm), wheat control (275 gm)	Men with prostate Ca on no active treatment (18): bran (10), placebo (8); randomized, placebo controlled single blind pilot study; intervention: 3 wks; followup: none	PSA: no difference in the mean change between rye and placebo based on 14.8 ± 9.1 to 14.7 ± 9.0 ng/ml for rye and 13.2 ± 10.9 to 13.2 ± 10.1 ng/ml for placebo (p >0.05) PSADT: not available
Parsons et al[22,23]	Plant based diet: 7 servings vegetables (2 cruciferous, 2 tomato products and 3 other vegetables), 2 servings whole grains, 1 serving legumes	Men with prostate Ca on active surveillance alone (42)[23]: plant based diet (29), control (13) or combined with men who completed primary treatment (69)[22]: plant based diet (45), control (24); intervention: 6 mos; followup: none	PSA (secondary end point): no difference between plant based diet and control for active surveillance alone based on 7.21 ± 4.14 to 9.49 ± 12.90 ng/ml in the intervention group and 6.94 ± 6.55 to 6.88 ± 6.98 ng/ml in controls (p = 0.21) or when analyzed in combination with men who completed primary treatment (no values provided) PSADT: not available
		Combined diet and dietary supplement trials	
Ornish et al[24]	Low fat (10% total calories) vegan diet: soy (1 serving tofu and 58 gm protein); fish oil (3 gm); vitamin E (400 IU); selenium (200 mcg); vitamin C (2,000 mg); stress reduction, exercise and group support	Men with prostate Ca on watchful waiting (90): intervention (41), control (49); randomized, controlled clinical trial; intervention: 12 mos; followup: none	PSA: Statistically significant difference in the mean change between intervention and control (−4% vs 6%, p = 0.016) based on a decrease from 6.23 ± 1.7 to 5.98 ± 1.7 ng/ml for intervention compared to an increase from 6.36 ± 1.7 to 6.74 ± 2.1 ng/ml in the control PSADT: not available
Kranse et al[18]	Margarine (20 gm) containing vitamin E (50 mg), selenium (200 mcg), green tea (6 cups), isoflavones (100 mg), lutein (10 mg), lycopene (10 mg), carotenoids (10 mg)	Men with prostate Ca with increasing PSA after primary treatment or watchful waiting (32): Group 1 (15), Group 2 (17); randomized, placebo controlled, double-blind, 2-arm crossover study; intervention: 6 wks; followup: 8 wks after period 2 intervention	PSA: not available PSADT (log slope method): no difference in total PSADT based on 41 to 44 wks (p = 0.84); statistically significant increase in free PSADT based on doubling time of 68 wks to a half life of 13 wks (p = 0.02)
		Dietary supplement trials	
Ansari and Gupta[21]	Lycopene (4 mg)	Men with metastatic prostate Ca (54), lycopene supplement and orchiectomy (27), orchiectomy alone (27); randomized controlled clinical trial; intervention: 2 yrs; followup: none	PSA: statistically significant difference between the lycopene group compared with orchiectomy alone based on 9.02 ± 7.5 and 3.01 ± 1.9 ng/ml (p = 0.001); unclear if the analysis represents a comparison in the difference in mean change in PSA between groups or before and after analysis PSADT: not available
Kucuk et al[19]	Lycopene (30 mg)	Men with prostate Ca awaiting surgery (26): lycopene (15), control (11); randomized, placebo controlled phase II clinical trial; intervention: 3 wks; followup: 13–30 days	PSA: no difference in mean % change between lycopene and placebo (−18% vs 14%) based on 6.89 ± 0.81 to 5.64 ± 0.87 ng/ml for lycopene supplements and 6.74 ± 0.88 to 7.65 ± 1.78 ng/ml for placebo (p = 0.25) PSADT: not available
Schroder et al[20]	Soy isoflavones (62.5 mg), lycopene (15 mg), silymarin (160 mg), ascorbic acid (225 mg), α-tocopherol (75 mg), carotenoids (3 mg), bioflavonoids (19 mg), selenium (128 mcg), zinc (18 mg), calcium carbonate (1,148 mg), other	Men with prostate Ca with increasing PSA after primary treatment (42): Group 1 (22), Group 2 (20); randomized, placebo controlled double blind crossover study; intervention: 10 wks followed by 4-wk washout period prior to crossover; followup: none	PSA: no statistically significant difference in total (p = 0.076) or free (p = 0.988) PSA PSADT: statistically significant increase in free PSADT based on 1,150 vs 445 days (2.6-fold, p = 0.041) for the supplement vs control treated periods; no statistically significant difference observed in the intent to treat group (p = 0.089); no statistically significant carryover effect reported (p = 0.131)

Followup reported as time from the end of the intervention where relevant.
* Number of subjects reported as 28.
† Mean change in PSA from the manuscript data was calculated to be 11.4% vs 22.4%.
‡ Kumar, personal communication.

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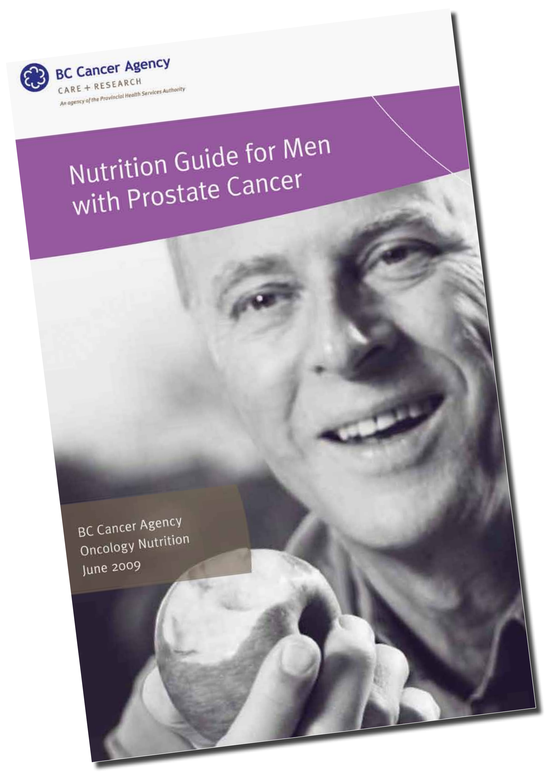
Results

The 62-page guidebook and shorter 12-page "newsletter-style" summary version (on display) were finalized in late 2009 and 500 hard copies of the guidebook were printed from donated funds from the Prostate Cancer Foundation BC and the BC Cancer Agency Genitourinary (GU) Tumour Group (a multidisciplinary practice group). The guidebook is currently being distributed to every newly diagnosed man with prostate cancer in British Columbia, Canada, within an innovative Prostate Cancer Kit supported by Prostate Cancer Foundation BC (www.prostatecancerbc.ca). The dissemination of the guidebook also includes availability to individual patients treated within the five provincial cancer centres of the BC Cancer Agency and various community-based oncology clinics. Lastly, it is also available as a free download from the internet from various websites including the BC Cancer Agency (www.bccancer.bc.ca) and Pro Can Support (www.procansupport.com).

Conclusions

An evidence-based nutrition guidebook for men with prostate cancer was developed and implemented by a multidisciplinary cancer care team in partnership with community-based support groups and stakeholders. This was undertaken to address the unmet need for nutrition resources for men with prostate cancer. The future directions for this project will be to evaluate the dissemination and uptake of the guidebook and its potential to influence lifestyle behaviours in prostate cancer survivors. Revisions to the content will also be required as new scientific data becomes available.



Selected Reference

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