



## The relationship between anxiety about prostate cancer among patients with biochemical cancer recurrence and the use of complementary and alternative medicines, diet, and exercise

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### Abstract

**Objective:** We aimed to explore associations between anxiety and specific health behaviors such as complementary and alternative medicine (CAM), diet, and exercise among prostate cancer patients.

**Methods:** PCa patients enrolled in a prospective cohort study of men with biochemical cancer recurrence were surveyed about use of CAM, diet, and exercise. Anxiety was measured with the Memorial Anxiety Scale for Prostate Cancer (MAX-PC) and the anxiety subscale of the Hospital Anxiety and Depression Scale.

**Results:** Nearly 70% (44 of 67) of the original cohort of patients completed the supplementary CAM survey. The mean age was 68 years. Eighty percent of respondents reported engaging in a relevant health behavior, and 64% reported doing so in direct response to their PCa diagnosis. Overall, the most prevalent specific behaviors were exercising (56%), making dietary changes (50%), taking calcium supplements (41%), and taking vitamin D supplements (39%). Elevated baseline PCa-specific anxiety (MAX-PC score >16) after biochemical cancer recurrence was associated with use of any CAM ( $P=0.01$ ), use of herbs/supplements ( $P=0.01$ ), and dietary changes ( $P=0.04$ ).

**Conclusion:** PCa patients commonly use CAM, dietary changes, and exercise in response to their diagnosis, and these changes are associated with elevated general and PCa-specific anxiety.

**Keywords:** Prostate cancer; complementary and alternative medicine; health behaviors; anxiety

### Introduction

Since the 1990s the use of complementary and alternative medicine (CAM) has grown in the United States, and a report from the 2012 cohort of the National Health Interview Survey found that 33% of American adults had used CAM in the previous 12 months [1]. CAM includes a variety of therapies, including herbs/supplements, acupuncture, yoga, and other nonconventional approaches. The rate

of CAM use among cancer patients appears to be equal to or higher than the rate in the general adult population, with an increasing trend in the past several decades from 25% to 49% [2]. Prostate cancer (PCa) patients have also been characterized as commonly using CAM, with prevalence estimates ranging from 8% to 90% with a mean of 30% in studies of patients with disease of different stages [3]. Additionally, PCa patients have

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been reported to incorporate other health behaviors such as diet and exercise behaviors after their diagnosis [4–6].

Studies have identified several correlates of the use of CAM, including higher income and education levels, younger ages, larger social networks, and specific psychological conditions [7–10]. Studies of cancer patients' psychological state have revealed a variety of potential factors that may influence CAM use, including anxiety, fear of recurrence, depression, emotional distress, and coping behavior [11–13]. Studies among PCa patients have found that anxiety can be an important factor in patients' decision-making process regarding treatment decisions [14–16]. This is increasingly recognized in patients with a biochemical recurrence (BCR) of PCa, which is an asymptomatic rise in prostate-specific antigen (PSA) level following initial therapy. Cancer-specific anxiety importantly influences those with BCR with regard to the timing of their decision to start androgen deprivation therapy (ADT), with patients with greater PCa-specific anxiety tending to start ADT earlier [17]. Specifically, identifying reasons for CAM use is important because these therapies could have potential risks as demonstrated by the SELECT trial, which found an increased risk of PCa among those randomized to receive vitamin E supplementation [18]. The influence of anxiety on patients' decisions to pursue use of CAM such as herbs and supplements, dietary changes, and exercise has not been investigated among men with BCR.

Aware of the effect anxiety can have on a patient's decision-making process, we hypothesized that among PCa patients with a BCR, those with higher PCa-specific anxiety levels would be likelier to report CAM use, dietary changes, and exercise in the hope of improving their health or prognosis. The aims of this study were (1) to measure the prevalence of an array of different health behaviors (CAM, diet, and exercise) among a sample of men with BCR, and (2) to investigate the specific relationship between PCa-specific anxiety and the use of CAM, diet, and exercise.

## Methods

Men who had undergone primary therapy (prostatectomy or radiation therapy) for PCa and then experienced BCR but who had not yet started ADT were approached to participate in a prospective cohort study at the time of their initial

appointment at the University of Chicago's Genitourinary Medical Oncology Clinic [17]. Patients were eligible if they had at least two increases in their PSA level a minimum of 2 weeks apart and had no radiographic evidence of PCa [19]. Informed consent was obtained according to institutional guidelines, and the protocol was approved by the University of Chicago Biological Sciences Division Institutional Review Board.

For the current study, an approved amendment was added to the original protocol so as to collect additional information regarding health behaviors and CAM use. On enrollment in the original study, patients completed a baseline questionnaire, and additional questionnaires were completed after each follow-up physician appointment until initiation of ADT [20]. We surveyed patients in the original cohort to complete an additional questionnaire regarding health behaviors, including CAM use, dietary changes, and exercise. This questionnaire was completed at follow-up appointments or by mail if the patient had already completed the study. Details on the participants and methods of the original study have been published elsewhere [17]. This analysis was not designed as part of the original study, and thus is secondary in nature.

## Measurements

The patients' demographic characteristics were available from the original study [17], as were the patients' psychological state and physical functioning scores, which had been assessed with validated instruments, including the Memorial Anxiety Scale for Prostate Cancer (MAX-PC) and the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) [21–24]. A MAX-PC PCa-specific anxiety subscale score of more than 16 was considered to be elevated and a HADS-A score of more than 8 was considered to represent an elevated general anxiety level [21–23, 25]. Clinical data were extracted from the medical records, including the patients' Gleason scores, PSA values, previous treatments, comorbid conditions, and medications.

The CAM questionnaire was designed on the basis of the frequent use of CAM and other health behaviors reported in previous studies of PCa patients [20, 26–28]. Specifically, patients were asked about (1) use of herbs and supplements (e.g., use of echinacea, saw palmetto, garlic, lycopene, soy,



green tea, megadose vitamins, selenium, vitamin E, calcium, vitamin D, or other supplements), (2) changes in their diet (e.g., change to a low-fat diet, increased soy intake, increased green tea intake, or other changes), (3) use of alternative medical systems (e.g., traditional Chinese medicine, naturopathic medicine, homeopathic medicine, or other systems), and (4) use of other CAM therapies and health behaviors (e.g., exercise, chiropractor, acupuncture, massage, prayer, support group, or other therapies). The questionnaire also asked about the timing and reasons for these health behaviors to understand if they were used before the original cancer diagnosis, following PCa diagnosis, and/or following BCR. Patients were also asked if they engaged in these health behaviors as a response to their PCa diagnosis or BCR. Finally, the questionnaire surveyed patients' communication patterns, decision-making processes, and monthly costs related to health behaviors.

### Statistical analysis

We analyzed use of CAM as follows: (1) use of any health behavior, including CAM, diet, and exercise; (2) use of any CAM therapies (excluding diet, exercise, and support groups); (3) use of herbs and supplements (e.g., vitamins, minerals, herbs, nutraceuticals); (4) use of other CAM therapies excluding herbs and supplements (e.g., acupuncture, massage); (5) making of dietary changes (e.g., increased green tea intake, low-fat diet); and (6) changes in exercise pattern. Participants were considered to have an elevated anxiety level if the MAX-PC PCa anxiety subscale score was more than 16 and if the HADS-A score was more than eight at the baseline as cut-offs as reported in previous publications [17, 24]. Associations between elevated anxiety and use of CAM, diet, and exercise were analyzed by a chi-squared test for univariate analysis. We considered  $P < 0.05$  as significant. All data analyses were performed with STATA SE 10.0 (StataCorp, College Station, Texas, United States).

## Results

### Patient characteristics

Sixty-nine percent (44/67) of the patients from the original study completed the questionnaire on CAM use and other health behaviors (Table 1). The respondents' mean age was 68 years (range 50–84 years, standard deviation 9.1 years),

and approximately one-quarter (21%) of respondents were African American. BCR was diagnosed in the patients a median of 58 months (range 1–175 months) before this study, and the patients had a median PSA level of 1.7 ng/mL (range 0.3–27.9 ng/mL) at the time of enrollment. Ninety-three percent of patients reported that their general health was good to excellent, and the patients had a MAX-PC PCa-specific anxiety subscale score of  $7.7 \pm 5.8$  and a HADS-A score of  $4.6 \pm 3.2$ , consistent with scores previously reported [21].

### Health behaviors and CAM therapies

Most respondents (80%) had engaged in at least one health behavior at some point in the past, and 61% did so before their original PCa diagnosis, which declined to 43% after BCR. Approximately two-thirds (64%) stated that at least one of these health behaviors was in direct response to their PCa diagnosis (rather than a therapy they used for other reasons before their PCa diagnosis). About two-thirds of patients (65%) were incorporating herbs and supplements, which was the most common type of CAM therapy. The use of herbs and supplements increased initially after PCa diagnosis but then declined after BCR, from 39% to 27% (Table 2).

With regard to specific therapies, an exercise program (56%), dietary changes (50%), taking of calcium supplements (41%), and prayer (33%) were the most prevalent (Table 2). The behaviors engaged in by most patients after PCa diagnosis were dietary changes (20%), taking of selenium supplements (18%), and engagement in an exercise program (16%). After BCR, dietary changes (23%), increasing dietary green tea intake (18%), and engagement in an exercise program (16%) were the most common behaviors. Overall, use of CAM, diet, and exercise was stable or declined after BCR. The only increase in health behavior after BCR was incorporation of green tea in the diet, but even this was a marginal increase in one participant. The behaviors most often used in response to PCa diagnosis in any timeframe were exercise (30%), use of calcium supplements (23%), drinking of green tea (23%), and taking of selenium supplements (18%). The mean monthly out-of-pocket cost for CAM use was \$46 dollars (range \$0–600). Supplements (e.g., green tea and garlic) and dietary changes were the modifications most often considered (22% and 11%



Table 1. Patient characteristics and comparison with nonresponders

Characteristic	Responders	Nonresponders
Age (years)	68±9.1	66±9.4
Education level		
High school degree or less	8 (19%)	4 (17%)
Associate degree or some college	8 (19%)	6 (26%)
Bachelor degree	12 (28%)	2 (9%)
Postgraduate degree	15 (34%)	11 (48%)
Race		
White	32 (78%)	17 (74%)
Black	9 (22%)	6 (26%)
Annual income (US dollars)		
≤50,000	11 (32%)	7 (35%)
50,001–100,000	12 (34%)	6 (30%)
>100,000	12 (34%)	7 (35%)
Self-reported health status		
Excellent	12 (28%)	4 (18%)
Very good	19 (44%)	12 (55%)
Good	10 (23%)	5 (23%)
Fair or poor	2 (5%)	1 (4%)
PSA level (ng/mL) <sup>a</sup>	1.7 (0.3–27.9)	1.6 (0.5–70.5)
PSA level doubling time (months) <sup>a</sup>	11.5 (0–997)	13.8 (0–997)
Time to recurrence (months) <sup>a</sup>	58.0 (1–175)	39.5 (1–116)
Gleason grade		
Low (2–6)	21 (57%)	9 (44%)
Moderate (7)	12 (32%)	6 (28%)
High (8–10)	4 (11%)	6 (28%)
MAX-PC score <sup>a</sup>	7.7±5.8	12.2±9.4
HADS-A score <sup>a</sup>	4.0±3.4	5.0±3.8

HADS-A, Hospital Anxiety and Depression Scale anxiety subscale; MAX-PC, Memorial Anxiety Scale for Prostate Cancer; PSA, prostate-specific antigen.

<sup>a</sup>Median and standard deviation.

respectively) but not actually taken by patients, primarily because of the unclear benefits, lack of information, and the low interest in these therapies.

### Associations between anxiety and health behaviors

Generalized anxiety, as indicated by an elevated HADS-A score greater than 8, correlated with an increased use of herbs and supplements ( $P=0.04$ ), dietary changes ( $P=0.04$ ), and other CAM therapies ( $P=0.04$ ) (Table 3). After PCa diagnosis, an elevated general anxiety level was associated with

increased use of any health behavior ( $P=0.04$ ), the making dietary changes ( $P=0.01$ ), the starting of an exercise program ( $P<0.01$ ), and use of other CAM therapies ( $P=0.01$ ). In regard to PCa-specific anxiety (MAX-PC score >16), after the initial PCa diagnosis, no correlations were found with overall prevalence of any of the health behaviors, and it correlated only with dietary changes ( $P<0.01$ ). However, after BCR, an elevated PCa-specific anxiety level was associated with increased health behavior of any type ( $P=0.05$ ), CAM use in general ( $P=0.01$ ), use of herbs and supplements ( $P=0.01$ ), and dietary



Table 2. Prevalence of health behaviors and use of complementary and alternative medicine

Category	Lifetime prevalence	Number of patients			
		Before PCa Diagnosis	After PCa Diagnosis	After BCR	Directly related to PCa
All health behaviors	80% (35/44)	27 (61%)	22 (50%)	19 (43%)	28 (64%)
All CAM <sup>a</sup>	75% (33/44)	20 (45%)	18 (41%)	15 (34%)	24 (55%)
Herbs and supplements	66% (29/44)	14 (32%)	17 (39%)	12 (27%)	22 (50%)
Exercise	55% (24/44)	20 (45%)	7 (16%)	7 (16%)	3 (7%)
Dietary changes	50% (22/44)	9 (20%)	9 (20%)	10 (23%)	13 (30%)
Other CAM therapies <sup>b</sup>	41% (18/44)	10 (23%)	6 (14%)	5 (11%)	9 (20%)
Specific therapies					
Calcium	41% (18/44)	7 (16%)	6 (14%)	7 (16%)	10 (23%)
Vitamin D	32% (14/44)	2 (5%)	6 (14%)	5 (11%)	9 (20%)
Prayer	32% (14/44)	7 (16%)	6 (14%)	4 (9%)	5 (11%)
Increased green tea in diet	32% (14/44)	1 (2%)	6 (14%)	8 (18%)	10 (23%)
Selenium	27% (12/44)	2 (5%)	8 (18%)	6 (14%)	8 (18%)
Low-fat diet	27% (12/44)	7 (16%)	5 (11%)	4 (9%)	4 (9%)
Vitamin E	23% (10/44)	8 (18%)	3 (7%)	3 (7%)	1 (2%)
Lycopene	16% (7/44)	0 (0%)	5 (11%)	3 (7%)	6 (14%)
Increased soy in diet	16% (7/44)	1 (2%)	5 (11%)	4 (9%)	4 (9%)
Support group	16% (7/44)	1 (2%)	5 (11%)	4 (9%)	6 (14%)

BCR, biochemical recurrence; CAM, complementary and alternative medicine; PCa, prostate cancer.

<sup>a</sup>Excludes exercise, diet, and support groups.

<sup>b</sup>Includes acupuncture, massage, chiropractic, prayer/spiritual healing, homeopathic, naturopathic, traditional Chinese medicine, or other CAM therapies.

Table 3. Correlations between anxiety and overall use of any health behavior

Category	HADS-A			MAX-PC		
	Percentage of patients		<i>P</i>	Percentage of patients		<i>P</i>
	HADS-A score <8 ( <i>n</i> =37)	HADS-A score ≥8 ( <i>n</i> =7)		MAX-PC score <16 ( <i>n</i> =36)	MAX-PC score ≥16 ( <i>n</i> =8)	
All health behavior	76	100	0.14	78	88	0.53
All CAM use	70	100	0.10	72	88	0.36
Herbs and supplements	59	100	0.04	64	75	0.55
CAM other than herbs and supplements	43	86	0.04	14	30	0.23
Dietary changes	43	86	0.04	44	75	0.12
Exercise	50	86	0.08	55	63	0.67

changes ( $P=0.04$ ) (Tables 4 and 5). In regard to demographic analyses, those with a college degree or higher were likelier to engage in an exercise program at any time than those with less

than a college education (75% vs 25%,  $P=0.04$ ). No statistically significant correlations were found with income, race, or age.



Table 4. Correlations between anxiety and health behaviors after original prostate cancer diagnosis

Category	HADS-A			MAX-PC		
	Percentage of patients		P	Percentage of patients		P
	HADS-A score <8 (n=37)	HADS-A score ≥8 (n=7)		MAX-PC score <16 (n=36)	MAX-PC score ≥16 (n=8)	
All health behaviors	43	86	0.04	44	75	0.12
All CAM use	38	57	0.34	39	50	0.56
Herbs and supplements	35	57	0.27	36	50	0.47
CAM other than herbs and supplements	8	43	0.01	14	13	0.92
Dietary changes	14	57	0.01	11	63	<0.01
Exercise	8	57	<0.01	11	38	0.07

CAM, complementary and alternative medicine; HADS-A, Hospital Anxiety and Depression Scale anxiety subscale; MAX-PC, Memorial Anxiety Scale for Prostate Cancer.

Table 5. Correlation between anxiety and health behaviors after biochemical relapse

Category	HADS-A			MAX-PC		
	Percentage of Patients		P	Percentage of patients		P
	HADS-A score <8 (n=37)	HADS-A score ≥8 (n=7)		MAX-PC score <16 (n=36)	MAX-PC score ≥16 (n=8)	
Any health behavior	38	71	0.10	36	75	0.05
CAM use	30	71	0.04	28	75	0.01
Herbs and supplements	22	57	0.05	19	63	0.01
CAM other than and supplements	8	11	0.12	11	13	0.91
Dietary changes	19	43	0.17	17	50	0.04
Exercise	8	57	<0.01	11	38	0.07

CAM, complementary and alternative medicine; HADS-A, Hospital Anxiety and Depression Scale anxiety subscale; MAX-PC, Memorial Anxiety Scale for Prostate Cancer.

### Decision making and communication regarding health behaviors and CAM

The most commonly reported sources of information about CAM use and other health behaviors were physicians (64%), print media (50%), and friends (33%). Although physicians were often reported as information sources, approximately two-thirds of patients (67%) indicated that the decision to pursue these interventions was entirely their own. The most commonly reported reasons for pursuing health behaviors and CAM use were “a desire to improve overall health” (88%), a desire to “do everything possible to treat cancer” (58%),

and a belief that these therapies had few side effects (50%) (Table 6). Other reasons given for CAM use and engaging in other health behaviors included a desire to use a more holistic approach to health care (29%), a desire to have a sense of control over medical care (29%), and the hope that the therapies would help with treatment-related side effects (28%). Half of the participants told at least one physician about some or all of their health behaviors and CAM therapies. The reasons most commonly given for nondisclosure were that the physician never asked the patient (44%) and a lack of time to discuss the topic (28%).



Table 6. Reasons reported for health behaviors and use of complementary and alternative medicine

Reasons	Percentage of patients <sup>a</sup>
Improve overall health	88
Do everything to treat cancer	58
Therapy had few side effects	50
Greater sense of control	29
More holistic approach	29
Help with treatment-related side effects	28
Help treat side effects related to cancer	21

<sup>a</sup>Among participants who answered this question.

## Discussion

We found that PCa patients with BCR commonly incorporate health behaviors including CAM, diet, and exercise, with many doing so specifically in response to their PCa diagnosis and recurrence. Many of these health behaviors declined after PCa diagnosis and BCR, with only dietary changes, vitamin D supplementation, selenium intake, and green tea intake in the diet increasing after diagnosis. Another important finding is that patient anxiety, as measured by the MAX-PC (PCa specific) and HADS-A (general), correlated with a significantly increased use of several health behaviors, including use of CAM therapies in this population.

While several articles have reported the use of CAM in PCa patients, ours is the first to report on its use in patients with a BCR along their cancer clinical continuum – before PCa diagnosis, after PCa diagnosis, and after BCR [8, 20, 26–38]. Most studies have examined CAM use overall or at a single point in time, usually after cancer diagnosis. One study examined urologic patients before and after surgery and found an increase in the utilization of CAM after surgery, from 30 to 53 among a total of 172 participants. Conversely, we found overall use of health behaviors and CAM declined after initial diagnosis, and further investigation is needed to assess these differences.

Only one prior study included a psychometrically validated instrument for anxiety in patients with localized PCa [8], and no prior study of these health behaviors among PCa patients used a PCa-specific anxiety scale, such as the MAX-PC. In that study, anxiety and depression were measured with the Profile of Mood States, and it did not predict CAM use among

patients with localized PCa who underwent therapy [39]. Our results indicate that anxiety could potentially play a role in increasing PCa patients' pursuit of specific health behaviors such as CAM use, dietary change, or exercise initiation. This study is unique in that our patients represent a carefully defined clinical scenario – patients in whom a BCR has just been diagnosed – a time when patients are often anxious and uncertain, and therefore likelier to take action as a consequence [17].

We found that PCa patients typically chose to pursue health behaviors including CAM use on their own, and only half of them talked with their physicians about these decisions. Many of these behaviors, especially dietary and exercise changes, are beneficial for improving overall health, and growing evidence in PCa, breast cancer, and colon cancer indicates that these lifestyle changes may lead to decreased disease recurrence [40–45]. The use of calcium and vitamin D is common advice for patients receiving ADT because of the risk of osteoporosis. However, some CAM therapies, such as supplementation with vitamin E, selenium,  $\beta$ -carotene, and multivitamins, have unproven benefits in PCa treatment, and in some instances can have potential harmful effects [46–49]. If patients are interested in improving their overall health, which was the reason most commonly cited for pursuing health behaviors such as CAM use, then improving diet and improving exercise patterns are the most important behavior changes that should be addressed. A lack of information was a common reason not to pursue these health behaviors, and thus such a discussion about health behaviors could help patients to make a better decision to improve their health.

Patients with a BCR of PCa and high PCa-related anxiety levels may be particularly eager to discuss modification of their lifestyle with their physicians. Health care professionals should take this opportunity to provide education on how diet and exercise will impact the patient's overall health and possibly the course of the cancer. Additionally, PCa patients who start ADT are at risk of long-term side effects, such as sarcopenia, diabetes, and heart disease, and CAM and lifestyle changes may help prevent the development of these conditions [50, 51]. However, clinicians should also counsel patients that interventions, such as use of multivitamins and other supplements, may carry risks [46, 48, 52].

There are limitations to our pilot study. Because the sample was small, with data collected at a single academic



center, the generalizability of our findings, while intriguing, is limited. This study was conducted among a cohort of men with BCR of PCa, which also limits generalization to other cancer types and to women. Our survey was based on retrospective self-report, and is at risk of recall biases; therefore prospective studies following patients' CAM use longitudinally are needed. The response rate of 69% is reasonable but not ideal; fortunately, the nonresponders do not appear to be substantially different than those who responded (Table 1). In fact, they appear to be slightly more anxious, making our findings conservative.

In summary, we found that PCa patients with a BCR of PCa commonly engage in health behaviors such as CAM use, dietary changes, and exercise initiation in response to their diagnosis. We also found that those with elevated general anxiety and PCa-specific anxiety have higher rates of health behaviors, including CAM use. Signs of anxiety may also present a cue to physicians that there is an important opportunity to educate patients about health behaviors that will lead to improved overall health, such as exercise, calcium, and vitamin D use. Using validated cancer-specific anxiety instruments such as the MAX-PC in larger, prospective studies will help provide more accurate information regarding a possible causal role of anxiety in the decision to pursue health behaviors and CAM therapies. Oncologists should ask about patients' health behaviors and CAM use that may impact their clinical outcomes.

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### Conflict of interest

The authors declare no conflict of interest.

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### Significance statement

This study among prostate cancer patients highlights the high prevalence of complementary and alternative medicine (CAM), diet, and exercise. These prevalence rates appear to vary depending on when patients are diagnosed and have a recurrence of their prostate cancer. An elevated anxiety level may be a factor in a patient's decision to utilize CAM, diet and exercise. For clinicians treating patients with prostate cancer, inquiries into these specific health behaviors are important. Increasing research is showing that diet and exercise may improve clinical outcomes including recurrence and survival in many cancer types including prostate cancer. Thus, there may be an opportune time after diagnosis and/or after recurrence of prostate cancer to advise patients about these health behaviors.

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