

A Handbook of Integrative Cancer Care Options and the Research Behind Them

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Quick Reference to Integrative Therapies

Eating Well

- Follow the Mediterranean diet or other plant-based, whole-foods diet:
 - * Use cold-pressed (extra-virgin) olive oil, especially to replace butter and other animal fats
 - * Eat fish high in omega-3 fatty acids: sardines, wild salmon and anchovies
 - * Eat more cruciferous vegetables: broccoli, cabbage, kale, cauliflower, Brussels sprouts, kohlrabi
 - * Eat food sources of lycopene: cooked tomatoes, strawberries, watermelon, pink grapefruit, guava and papaya
 - * Eat less red meat, cooking it at a low temperature
 - * Avoid eating smoked and cured meats
 - * Reduce saturated fats, found in dairy foods, meat and lard
 - Avoid whole-milk products (milk, cheese, butter)
- Eat organic soy foods, such as tofu and fermented miso and tempeh
- Drink green tea
- Drink pomegranate juice
- Add freshly ground flaxseed to foods

Sharing Love and Support

- Draw from or develop a social support network if possible :
 - * Support groups
 - Supportive-expressive therapy
 - * CBT social skills training

Exploring What Matters Now

- Find your comfort level regarding your involvement in making decisions about treatment
- Draw on spiritual connections if you find comfort and support in them
- Get informational support, involving your partner if you have one

See BCCT.ngo for more details about benefits and cautions regarding each therapy.

7 Healing Practices



Moving More

 Engage in vigorous activity causing sweating and increased heart and respiratory rates

Managing Stress

Mind-body approaches:

- Meditation
- Relaxation techniques
- Yoga
- Music therapy
- Tai chi
- Hypnosis
- Expressive art techniques

Creating a Healing Environment

- Increase exposures to green natural areas and sunlight (mindful of skin cancer risks)
- Reduce exposures to chemicals including pesticides, dioxins, PAHs and solvents

Natural Products

Managing Side Effects & Promoting Wellness	Reducing Risk	See BCCT.ngo for more
Cranberry juiceMedical cannabis and cannabinoids	Grape seed extractLycopeneQuercetin	aetails about benefits and cautions regarding each therapy.

Items in bold are in more than one category, and those in green are in all three.

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Most of the off-label drugs here require a prescription from a licensed physician, and all require medical supervision and monitoring.

Treating the Cancer

- Chronomodulated therapy
- Bisphosphonates
- Metformin

Managing Side Effects and Promoting Wellness

- Metformin
- Chronomodulated therapy

Reducing Risk

• Metformin

Other Approaches

Mind-body approaches for managing side effects:

- Qigong/tai chi during radiation
- Yoga

Body-manipulative therapies for managing side effects:

• Acupuncture

Energy therapies for managing side effects:

• Reiki

Bioelectromagnetically based therapies for managing side effects:

• Transcutaneous electrical nerve stimulation (TENS)

Healthy living for treating the cancer (promoting survival) and reducing risk:

- Maintain a healthy body weight or lose weight if overweight
- Quit smoking tobacco

Investigational Therapies

These therapies show promise, but **research does not yet show good evidence of effectiveness**. *Items in bold are in more than one category.*

Treating the Cancer

- Green tea extract
- Isoflavones, including soy supplements and red clover
- Lycopene
- Modified citrus pectin
- Omega-3 fatty acid supplements containing DHA and EPA
- Pomegranate fruit and extract
- Pomi-T
- Zyflamend: mixture of rosemary, turmeric, ginger, holy basil, green tea, hu zhang, chinese goldthread, barberry, oregano, baikal skullcap
- Low-dose naltrexone (LDN)

Managing Side Effects and Promoting Wellness

- Aged garlic extract
- Melatonin and circadian activity/sleep cycle integration
- Omega-3 fatty acid supplements containing DHA and EPA
- Vitamin A (retinol)
- Intravenous vitamin C
- Chronomodulated therapy
- Hyperbaric oxygen therapy

Reducing Risk

- Green tea extract
- Soy isoflavones

Conventional Therapies

Conventional therapies for treating the cancer and managing side effects are widely available; ask your doctor for information.

Key Points

- Less aggressive options in prostate cancer treatment have become available. in recent decades, preserving quality of life for many men without sacrificing survival.
- Radical surgery and/or radiation therapy are no longer standard approaches in conventional treatment for early, low-risk prostate cancer, with a shift toward watchful waiting or active surveillance.
- Integrative therapies during a period of waiting or surveillance, and also during treatment, show significant potential benefit to patients.
- We provide examples of different integrative approaches to prostate cancer care.
- Rather than "watchful waiting" alone for low-risk prostate cancer, engaging in an active surveillance program including complementary therapies often brings benefit.
- The 7 Healing Practices listed all promote wellness and tend to make your body terrain less hospitable to the development and progression of cancer. Some practices address cancer symptoms and side effects. These practices:
 - Eating Well
 - Moving More
 - Managing Stress
 - Sleeping Well
 - Creating a Healing Environment
 - Sharing Love and Support
 - Exploring What Matters Now
- Increased prostate cancer risk has been linked to diet and lifestyle factors including a high-fat diet, obesity and a sedentary lifestyle.
- Beyond the 7 Healing Practices, complementary therapies and lifestyle practices can be useful to enhance treatment effects, improve quality of life and possibly even extend life for those with prostate cancer.
- We present natural products and off-label, overlooked and novel cancer approaches (ONCAs) in six groups:
 - 1. Good clinical evidence of efficacy & safety, easy access
 - 2. Good clinical evidence of efficacy & safety, limited access
 - 3. Limited clinical evidence of efficacy but good safety, used in leading integrative programs
 - 4. Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit
 - 5. Especially promising preclinical evidence of efficacy and safety
 - 6. Evidence of no efficacy or may be dangerous
- Therapies and approaches are evaluated according to their effects:
 - 1. Treating the cancer
 - 2. Managing side effects and promoting wellness
 - 3. Reducing risk
 - 4. Optimizing your terrain
- Novel diagnostic tests specific for prostate cancer are available.
- Some integrative oncology clinicians report encouraging success in extending survival and improving quality of life in individuals with advanced prostate cancer.

Introduction

Prostate cancer is a prime example in which an integrative approach may be incorporated not only for reducing the risk of primary prostate cancer, but in treating and reducing risk of progression or recurrence. Following a healthy lifestyle program during active surveillance of low-risk prostate cancer may favorably change the behavior of the cancer while at the same time improving health and quality of life. Holding the cancer in this low-risk state could mean foregoing invasive treatments such as surgery or radiation therapy—treatments that can significantly reduce quality of life.

In the ProtecT study, for instance, men with localized prostate cancer and favorable prognoses who were followed for 10 years lived equally long whether they did active surveillance, surgery or radiation therapy. While the disease was less likely to progress in those receiving prostatectomy or radiotherapy, 44 percent of the patients who were assigned to active monitoring did not receive radical treatment and avoided side effects. Moreover, survival was as good among those who were untreated as among those who were treated—and they avoided the risks of treatment side effects.

Men with newly diagnosed, localized prostate cancer need to consider the critical tradeoff between the short-term and long-term effects of radical treatments on urinary, bowel and sexual function and the higher risks of disease progression with active monitoring, as well as the effects of each of these options on quality of life."¹

Whatever conventional treatment option turns out to be right for you, there is a role for wisely integrating complementary therapies. We give you information on those therapies that have evidence for benefit: lifestyle practices, natural products and off-label, overlooked or novel cancer approaches (ONCAs). We will focus on two lifestyle programs for men in active surveillance, Ornish Lifestyle Medicine created by Dean Ornish, MD, and the Active Holistic Surveillance program of Aaron Katz, MD. We hope in your exploration you find that you have choices in living more healthfully and fully with prostate cancer.

Michael Lerner

Watchful Waiting

Watchful waiting and active surveillance are treatments used for older men who do not have signs or symptoms or have other medical conditions and for men whose prostate cancer is in early stages and progressing slowly.

Watchful waiting is closely monitoring a patient's condition without giving any treatment until signs or symptoms appear or change. Treatment is given to relieve symptoms and improve quality of life.

Active surveillance is closely following a patient's condition without giving any treatment unless test results change. It is used to find early signs that the condition is getting worse. In active surveillance, patients are given specific exams and tests to check if the cancer is growing: digital rectal exam, prostate-specific antigen (PSA)

test, transrectal ultrasound and transrectal needle biopsy. Treatment is given when the cancer progresses.

Other terms describing no active treatment to manage prostate cancer right after diagnosis:

- Observation
- Watch and wait
- Expectant management

Integrative Care in Prostate Cancer

In the ProtecT study, men with localized prostate cancer and favorable prognoses who were followed for 10 years lived just as long whether they did active surveillance, surgery or radiation therapy.

Before investigating integrative care in prostate cancer, we recommend reviewing integrative cancer care in general.

Our goal is to help you live as well as you can for as long as you can, using the optimal combination of conventional, complementary and integrative therapies and approaches.

Cancers are composed of cells that divide without stopping and do not die as programmed. Some divide slowly, others quickly. Some are more invasive than others. Body terrain can influence the microenvironment in which the cancer exists, making it more or less likely to spread. You can sometimes improve your body terrain with integrative practices. (See Body Terrain and the Tumor Microenvironment)

Knowing how your cancer behaves will influence the type of testing and treatment used, prepare you for possible treatment side effects and guide you in steps to prevent or minimize these effects. It will help you understand and choose the complementary therapies and lifestyle approaches that may enhance your conventional treatment, manage side effects and improve your quality of your life.

You can also prepare your home team for what to expect. You can plan ahead to line up the support you may need. You can anticipate side effects and work to minimize them even before treatment starts. Finally, learning what to expect allows you to prepare mentally and spiritually to catalyze your resilience for facing the weeks and months to come.

You may read "the median five-year survival for this cancer is X percent." That means that this percentage of people survive at least five years. The five-year survival rate for most men with local or regional prostate cancer is nearly 100 percent. For men diagnosed with prostate cancer that has spread to other parts of the body (metastasized), the five-year survival rate is 30 percent.² Survival may also be expressed as median survival time—usually in years—meaning half of patients with a similar diagnosis will be alive at that time.

But median survival doesn't show the range of survival expectancy—which can vary from months to decades. We know many people who have lived far beyond the median.

Getting healthier with cancer—and skillful use of conventional and complementary therapies—may help extend your life. It will very likely improve the quality of your life. There is nothing wrong with hope.

Clinical Practice Guidelines

- National Comprehensive Cancer Network:
 - Professional Guidelines, www.nccn.org/professionals/physician_gls/pdf/prostate.pdf (Login required)
 - Guidelines for Patients: Prostate Cancer, www.nccn.org/patients/guidelines/prostate/index.html
- American Society of Clinical Oncology: Genitourinary Cancer, www.asco.org/practice-guidelines/quality-guidelines/guidelines/genitourinarycancer



Examples: Treatment Approaches from Noted Specialists and Practices

We note examples of prostate cancer treatment approaches used by leaders in the field. Some use minimally invasive conventional procedures with some integrative approaches, while others are more fully integrative in approach.

Aaron Katz, MD, and the Active Holistic Surveillance Program

Aaron Katz, MD, is a urologist specializing in prostate cancer. Known for his program of active holistic surveillance, Dr. Katz is also known for his work with cryotherapy (using cold temperatures therapeutically).³ Cryotherapy is a minimally invasive means of treating prostate cancer. Dr. Katz has published research demonstrating that by four years post cryotherapy, men receiving this treatment report a good quality of life comparable to those who underwent active holistic surveillance.⁴

For men with low-risk, early stage prostate cancer, Dr. Katz has developed a program in which his patients engage in lifestyle practices, such as diet, exercise and mindbody approaches, as well as take specific dietary supplements to decrease the risk of cancer progressing. As Katz explains:⁵

Active surveillance is an emergent strategy for management of indolent prostate cancer. Our institution's watchful waiting protocol, active holistic surveillance (AHS), implements close monitoring for disease progression along with various chemopreventive agents and attempts to reduce unnecessary biopsies.

In research of this approach, particularly the nutritional component, Katz and colleagues looked at treatment rates of men on their AHS protocol and determined reasons for progression. They analyzed survival rate, discontinuation rates and definitive treatments for low-risk and low-intermediate-risk patients enrolled in AHS at their center. They concluded that incorporating chemopreventive agents in their AHS protocol "has allowed patients to prolong definitive treatment for many years."⁵

In a later study, Katz and his colleagues reported results of a retrospective review comparing self-reported quality of life in men with prostate cancer who were treated with minimally invasive cryotherapy, cyberknife (CK) or active holistic surveillance (AHS). They looked at data over a four-year period and concluded that "after initially lower bowel habits and sexual function scores, CyberKnife or cryotherapy-treated patients had no significant difference in quality of life relative to AHS patients. These results highlight the benefit of CyberKnife and cryotherapy in the management of organ-confined prostate cancer."⁴ As a group, patients who choose minimally invasive treatment may expect some initial lower function, but their quality of life will eventually improve and be comparable to quality of life reported by AHS patients.

Ornish Lifestyle Medicine

Compared to men under active surveillance who didn't make lifestyle changes, those who followed Ornish's program had favorable biological markers, including lower PSAs.

Cardiologist Dean Ornish, MD, originally developed his Ornish Lifestyle Medicine program to reverse heart disease and has since adapted and studied the program in men with prostate cancer. The program looks at four elements of a person's life:

- What you eat
- How you respond to stress
- How active you are
- How much love and support you have

Simply put, the program urges you to "Eat well, stress less, love more, move more." (These are also four of our 7 Healing Practices.)

Most of this outpatient program happens outside the clinic in your everyday life. In response to criticism from some conventional practitioners, Dr. Ornish asks: "What's the more radical treatment: have a heart transplant (or prostatectomy) or walk, meditate, eat vegetables and quit smoking?"⁶

Even though the program "is considered experimental and investigational as a treatment for …prostate cancer",⁷ the evidence shows that adopting these healthy lifestyle changes provides benefit: compared to men under active surveillance who didn't make lifestyle changes, those who followed Ornish's program had favorable biological markers, including lower PSAs. Benefits are directly proportional to the degree of lifestyle changes made.⁶

Research highlights of the Ornish program in prostate cancer:⁸

- Slower progression or stable cancer in men with early stage prostate cancer (Gleason score less than 7) or low-risk prostate cancer:
 - Fewer men needing conventional treatments
 - Decrease in prostate specific antigen (PSA) compared to an increase in the control group
 - Inhibited prostate cancer cell growth
- Favorable gene expression
- Significant improvements in weight, abdominal obesity, blood pressure and lipid profiles
- Increased telomerase activity in peripheral-blood mononuclear cells (PBMCs)
- A rise in protective IGFBP-1

Challenges with the Ornish program:

- Following the program consistently,⁹ although Ornish says that hospitals and clinics using the Ornish Lifestyle Medicine Program are now reporting 85 to 90 percent of those completing the 9-week program are still following the program one year later.⁶
- Increased risk for deficiencies of vitamin B₁₂, vitamin E and zinc;¹⁰ these are manageable with medical supervision and perhaps supplementation
- Insurance coverage¹¹

Charles "Snuffy" Myers, MD

Dr. Charles "Snuffy" Myers is a noted medical oncologist and prostate cancer survivor who specializes in treating prostate cancer. He practices conventional oncology and also considers lifestyle practices, particularly diet, important for men with prostate cancer. He thinks deeply and innovatively about conventional prostate cancer treatment, such as targeted therapies, as well as the problem of prostate cancers becoming resistant to chemotherapy. He is now editor-in-chief of an information and resource website for those with prostate cancer, Prostapedia. He has also written a cookbook specifically for prostate cancer: *The New Prostate Cancer Nutrition Book*.

In his compelling presentation on Grand Rounds Urology, he discusses these topics and presents information on his group's study using a drug that inhibits the enzyme poly ADP ribose polymerase (PARP) in advanced prostate cancer patients who were no longer responding to the chemotherapy drug taxotere. Dr. Myers states:¹²

So 20 percent to 30 percent of post-taxotere patients may be candidates for PARP therapy, an oral drug associated with close to 90 percent response rate. So it's hard for me to believe this won't be an important advance in the management of those patients. In addition to being very well tolerated, this drug does not depend on testosterone presence or absence to work.

Prostate Oncology Specialists

Medical oncologists Mark Scholz, MD; Richard Lam, MD; and Jeffrey Turner, MD, run an integrative oncology practice in Marina del Ray, California. One of BCCT's advisors, a medical advocate, is impressed with their integrative, individualized approach. Doctors Scholz, Lam and Turner state:

As medical oncologists rather than surgeons, we do not have a preset agenda toward a specific treatment. All treatments, including active surveillance, hormone therapy, immunotherapy, surgery, radiation, brachytherapy, cryotherapy, focal therapy, proton therapy, nutritional and alternative therapies, HIFU and chemotherapy are given equal consideration depending on the unique needs of each individual patient.

Their Prostate Oncology Specialists website, books and publications provide a wealth of information on making decisions about prostate cancer treatment, and shedding light on innovative, integrative approaches to prostate cancer care. Find more information about their resources and publications below.

Prostate Institute of America

Dr. Duke Buhn with the Prostate Institute of America provides "options that include minimally invasive therapies, including cryotherapy, as a means of treatment that increase survivability and may reduce side effects and complications." According to one of BCCT's medical advocacy advisors, Dr. Buhn has been performing cryotherapy for prostate cancer for many years. He is also a master at noninvasive methods to gather information, such as Harmonic Doppler Ultrasound.

Block Center for Integrative Cancer Treatment

Keith Block, MD, integrates lifestyle, nutrition, natural products and other complementary approaches into conventional cancer care. At the 2003 conference of the American Society of Clinical Oncology, he presented a case series of 27 prostate cancer patients who began treatment with combined androgen blockade after diagnosis of distant metastases. All patients received conventional treatment along with counseling in therapeutic nutrition and supplementation, fitness and physical therapy, and mind-spirit care. Both survival after severe disease and survival after development of androgen-resistant disease exceeded observations of similar groups in the literature.¹³



Integrative Programs, Protocols and Medical Systems

Programs and protocols related to prostate cancer:

- Alschuler & Gazella complementary approaches: Alschuler LN, Gazella KA. *The Definitive Guide to Cancer, 3rd Edition: An Integrative Approach to Prevention, Treatment, and Healing.* Berkeley, California: Celestial Arts. 2010; Alschuler LN, Gazella KA. *The Definitive Guide to Thriving after Cancer.* Berkeley, California: Ten Speed Press. 2013.
- Block program: Block KI. *Life over Cancer: The Block Center Program for Integrative Cancer Treatment.* New York: Bantam Dell. 2009.
- Chang strategies: Chang R. *Beyond the Magic Bullet: The Anti-Cancer Cocktail.* New York: Square One Publishers. 2012.
- Cohen & Jefferies Mix of Six anticancer practices: risk reduction Cohen L, Jefferies A. *Anticancer Living: Transform Your Life and Health with the Mix of Six.* New York: Viking. 2018.
- Elsegood LDN guidelines: Elsegood L. Ed. *The LDN Book*. Vermont: Chelsea Green Publishing. 2016.
- Geffen Seven Levels of Healing: Geffen J. *The Journey through Cancer: An Oncologist's Seven-Level Program for Healing and Transforming the Whole Person.* New York, New York: Three Rivers Press. 2006.
- Lemole, Mehta & McKee prostate cancer protocol: Lemole G, Mehta P, McKee D. *After Cancer Care: The Definitive Self-Care Guide to Getting and Staying Well for Patients with Cancer.* New York, New York: Rodale, Inc. 2015.
- McKinney prostate cancer protocol: McKinney N. *Naturopathic Oncology, 3rd Edition.* Victoria, BC, Canada: Liaison Press. 2016.
- Ornish Lifestyle Medicine, http://deanornish.com/ornish-lifestyle-medicine/

Integrative Therapies in Prostate Cancer



7 Healing Practices: The Foundation

The 7 Healing Practices listed here all promote wellness and tend to make your body terrain less hospitable to the development and progression of cancer. Some practices address cancer symptoms and side effects.



Eating Well

Choices in diet are associated with prostate cancer outcomes.

Treating the Cancer

Limited evidence shows a few

foods slow prostate cancer progression, reduce angiogenesis (creation of new blood vessels to supply tumor cells), induce cell death (apoptosis) and/or reduce metastasis:¹⁴

- Fish consumption for four to six weeks before surgery
- Coffee consumption before a prostate cancer diagnosis
- Cruciferous vegetables: broccoli, cauliflower, cabbage, Brussels sprouts, kale, mustard greens, and chard greens
- Pomegranate juice
- Soy foods (preferably organic), possibly in combination with tomato juice
- Cranberry juice
- Flaxseed
- Turmeric
- Rye bread versus wheat bread

Pomegranate juice has also been associated with longer PSA doubling times,¹⁵ although possibly only in men with the MnSOD AA genotype.¹⁶

A small trial of a dietary intervention showed lower PSA in patients with nonmetastatic prostate cancer after three weeks consuming tomato products.¹⁷

Other foods are associated with worse disease outcomes:18

- Whole milk products (but not low-fat varieties)
- Saturated fats from animal origins, including milk products and meats

Managing Side Effects and Promoting Wellness

Men with mild to moderate erectile dysfunction who drank pomegranate juice tended to report more favorable scores on the Global Assessment Questionnaire than men drinking a placebo. The result of this small pilot study was not statistically significant, nor were all the subjects cancer survivors.¹⁹

Reducing Risk

Studies have found these associations between food choices and prostate cancer or aggressive prostate cancer at diagnosis:²⁰

Higher Risk	Lower Risk
 Dairy and high calcium intake* Processed red meat, such as salami, bologna, sausage, bacon and hot dogs Eggs/choline Poultry (with skin) Animal fat/saturated fat Salted or smoked fish 	 Fish, especially fish with high levels of omega-3 fatty acids such as salmon, sardines, mackerel and herring∞ Tomatoes/lycopene Fats from vegetable sources, especially olive oil and nuts Cruciferous vegetables: broccoli, cauliflower, cabbage, Brussels sprouts, kale, mustard greens, and chard greens Coffee Soy foods or soy protein: soy isoflavones daidzein and genistein are both associated with lower risk, as is heat-treated soy grits Tea, especially green tea Low-carbohydrate diet Vitamin E† Flavonoids found in chocolate, green and black tea, beans, cherries, strawberries, cocoa, onions and apples Plant sterols

* Higher levels of calcium intake have been more strongly associated with increased risk of aggressive prostate cancer in men of African-American descent and individuals with a low body mass index (BMI) compared to men of European-American descent or those with higher BMIs.²¹ Men taking in more than 2000 mg of calcium a day combined food and supplements—have a higher risk of lethal prostate cancer, but the link may be due to phosphorus, which is found along with calcium in dairy foods as well as thousands of foods with phosphate-containing additives.²²

 $\infty Reduced risk may be modified by genetic variation in the COX-2 gene^{23} and by the specific fatty acids consumed. ^{24}$

[†] Higher amounts of dietary vitamin E consumed by prostate cancer patients of European-American descent were associated with less aggressive forms of the disease. This was not seen in patients of African-American descent.²⁵

Dietary vitamin D intake, mostly from dairy foods, was not related to prostate cancer risk in large pooled meta-analyses. 26

Food Recommendations

Some of the more conservative cancer information services downplay the role of diet in prostate cancer, such as the American Society of Clinical Oncology's statement: "There is not enough information right now to make clear recommendations about the exact role eating behaviors play in prostate cancer. Dietary changes may need to be made many years earlier in a man's life to reduce the risk of developing prostate cancer."²

We disagree. Although all the mechanisms and details are not understood (they seldom are in science), enough evidence has emerged to make recommendations. The risks of following these recommendations are very low. Because benefits from these recommendations extend to heart disease and other chronic conditions in addition to many types of cancer, the potential benefits are enormous.

In general, following a plant-based, whole-foods diet such as the Mediterranean diet provides benefit:

- Use cold-pressed (extra-virgin) olive oil, especially to replace butter and other animal fats
- Eat fish high in omega-3 fatty acids: sardines, wild salmon and anchovies
- Eat more cruciferous vegetables: broccoli, cabbage, kale, cauliflower, Brussels sprouts, kohlrabi
- Eat food sources of lycopene: cooked tomatoes, strawberries, watermelon, pink grapefruit, guava and papaya
- Eat less red meat: "Choose lean meat derived from grass-fed animals. Eat it sparingly and prepare the proteins at a low temperature."²⁷
- Avoid eating smoked and cured meats.
- Reduce saturated fats, found in these foods:
 - Dairy foods: butter, cream, ghee, whole milk and cheese
 - Meat: fatty cuts of beef, pork and lamb, chicken skin, and processed meats including salami and sausages
 - Lard
- Avoid whole-milk products (milk, cheese, butter)

In addition, these foods also show benefit:

- Soy foods, such as tofu and fermented miso and tempeh
- Green tea
- Pomegranate juice
- Flaxseed (freshly ground)

The risks from these lifestyle changes are very low, and the potential benefits are great.

Moving More

Treating the Cancer

In men with prostate cancer, three or more hours per week of vigorous activity is associated with a substantially lower risk of dying from prostate cancer compared with men with less than one hour of vigorous activity per week.²⁸

Managing Side Effects and Promoting Wellness

Men with prostate cancer managed with androgen deprivation therapy who engaged in long-term soccer (European football) training showed increased mineral density in their right femoral neck bones compared to men not training. However, over five years, muscle mass, knee-extensor muscle strength, VO₂ max, and postural balance decreased in both groups.²⁹

Reducing Risk

Strong evidence shows that vigorous activity (activities that cause sweating and increased heart and respiratory rates) is associated with a reduced risk of lethal prostate cancer. Activity such as brisk walking (three or more miles per hour) three times a week or regular bicycling is associated with a substantially lower risk of recurrence compared to lower frequency or more leisurely activity.³⁰

A Norwegian study following almost 2000 men for 30 years found that men in the highest third of fitness had an increased risk of prostate cancer compared to those in the lowest third.³¹ However, a much larger study following almost 50,000 men for 26 years found an opposite association with advanced and lethal prostate cancers: Men who engaged most frequently in vigorous activity over the length of the study had a 30 percent lower risk of developing advanced prostate cancer and 25 percent lower risk of developing lethal prostate cancer when compared with men who exercised the least.³²

Managing Stress

Treating the Cancer

In a large study in Sweden, men with the highest levels of perceived stress had a statistically significantly increased rate of prostate cancer-specific mortality.³³

Managing Side Effects and Promoting Wellness

A small study found that participation in a mindfulness-based stress reduction program was associated with "enhanced quality of life and decreased stress symptoms, altered cortisol and immune patterns consistent with less stress and mood disturbance, and decreased blood pressure."³⁴

Reducing Risk

Chronic inflammation, which can be provoked by chronic stress, is involved in prostate carcinogenesis.³⁵

Sleeping Well

Reducing Risk

Large studies in Sweden and Finland have found *no association* between sleep duration and risk of prostate cancer overall, or for advanced or more lethal disease.³⁶ Sleep does not seem to be an important factor in prostate cancer risk.

Creating a Healing Environment

Reducing Risk

A large study of twins concluded that inherited genetic profile can influence your risk of prostate cancer, but "the environment has the principal role in causing sporadic cancer."³⁷

Several chemical exposures are associated with increased risk of prostate cancer:³⁸

- Agent Orange
- Aromatic amines
- Dioxins
- Methyl bromide
- Organochlorine and other pesticides
- PAHs
- Solvents

A few exposures are associated with lower risk:

- Some evidence suggests that men living in greener areas, either recently or about a decade earlier, had lower risks of prostate cancer.³⁹
- Limited evidence suggests that exposure to sun is associated with reduced risk of prostate cancer.⁴⁰

Sharing Love and Support

Managing Side Effects and Promoting Wellness

Studies have found that social support is associated with prostate cancer patients' reports of quality of life.⁴¹

Exploring What Matters Now

Managing Side Effects and Promoting Wellness

Study results among men with newly diagnosed clinically localized prostate cancer:

- Men who were more active in making decisions about treatment and who had greater knowledge reported lower decisional conflict and higher decision-making satisfaction. They also reported greater decision-making difficulty.⁴²
- Greater spirituality was associated with greater decision-making satisfaction, less decisional conflict, and less decision-making difficulty.⁴³
- Receiving informational support (to couples) facilitated treatment decision making and was associated with lower levels of psychological distress.⁴⁴

Other Lifestyle Associations: Healthy Living

Obesity

High body mass index (BMI) "is strongly associated with increased risk of developing lethal prostate cancer, and increasing evidence suggests that obesity (either before or at the time of diagnosis) is associated with prostate cancer progression and prostate

cancer-specific mortality."⁴⁵ Weight gain of five pounds or more from five years prior to one year after surgery is associated with a much higher risk of recurrence and prostate cancer-specific mortality. Another study found a 5 kg/m² increase in body mass index (BMI) was associated with a 20 percent higher risk of death from prostate cancer.⁴⁶

However, a large, 30-year Norwegian study found that lower BMI (under 25) was associated with a *higher* risk of prostate cancer compared to BMI at or greater than 25,³¹ contrary to most other evidence. We look forward to further research and analysis to explain this apparent contradiction.

The World Cancer Research Fund/American Institute for Cancer Research includes recommendations to "keep your weight within the healthy range and avoid weight gain in adult life" to reduce the risk of all cancers.⁴⁷

Tobacco Smoking

According to Meir Stampfer at Harvard, of the risk factors that you can change, "smoking within the previous 10 years is one of the big ones."⁴⁸ A 2018 study found that "current smokers at the time of primary curative treatment for localized prostate cancer are at higher risk of experiencing biochemical recurrence, metastasis, and cancer-specific mortality."⁴⁹ Studies have consistently found worse outcomes among smokers compared to nonsmokers in prostate cancer patients treated by radiation, androgen-deprivation therapy (ADT), and radical prostatectomy.⁵⁰

Beyond the 7 Healing Practices: Further Integrative Therapies

Complementary therapies and lifestyle practices can be useful to enhance treatment effects, improve quality of life and possibly even extend life for those with prostate cancer.

Several therapeutic approaches show potential. The therapies presented here are not necessarily singly or in combination the right supplements for you to use. This list is not a recommendation from BCCT. Refer to our summaries of each of these therapies to see uses in prostate cancer, where to find dosing guidelines, cautions, and their use in integrative protocols, programs and systems. A licensed health professional experienced in integrative prostate cancer care can provide valuable guidance in selecting therapies.

Therapies are grouped according to their effects:

- Treating the cancer
- Managing side effects and promoting wellness
- Reducing risk
- Optimizing your terrain

We present natural products and off-label, overlooked and novel cancer approaches (ONCAs) in six groups:

- 1. Good clinical evidence of efficacy & safety, easy access
- 2. Good clinical evidence of efficacy & safety, limited access
- 3. Limited clinical evidence of efficacy but good safety, used in leading integrative programs

- 4. Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit
- 5. Especially promising preclinical or emerging clinical evidence of efficacy and safety
- 6. Evidence of no efficacy or may be dangerous

Within each section, we list only groups containing applicable therapies.

Other integrative therapies and approaches are described but not categorized. See the full summaries as linked for more information on each of these therapies.

Finding Reliable Information about Prostate Cancer

As research continues to identify best practices in prostate cancer prevention, detection and treatment, advice has changed considerably over the last couple of decades.

However, quite a lot of information that is either outdated or inaccurate is still available online and is passed along through social media.

A 2018 study evaluated the accuracy of 150 videos on prostate cancer screening and treatment posted on YouTube. Study findings:⁵¹

- Few videos provided summaries or references or even defined medical terms.
- Videos with lower scientific quality were actually met with *higher* viewer engagement: more views and more "thumbs up" ratings and comments.
- Comments often contained advertising and peer-to-peer medical advice.

We encourage our readers to check the dates on information, cross-check claims with reliable and authoritative science-based sources, and validate claims as far as possible before investing much time or money in miracle cures.

Cells, Animals and People

Studies on human cells can be helpful in finding effects of drugs, radiation, natural compounds and other potential therapies on tumors. However, isolated cells or tissues in a highly controlled lab may behave very differently from tumors and other cells in real human beings.

Drawing conclusions from cell studies is fraught with the potential for errors, a little bit like predicting children's final career successes from their performance in kindergarten. Yes, some differences hold all throughout the many levels and experiences on the way to the final goal, but many other intervening variables can change the outcome.

Animal studies are a step up from cell studies, but differences between humans and lab animals make animal evidence unreliable in predicting how cancer patients will respond to therapies that work well with animals.

While cell and animal studies are good markers for therapies to explore further, these results alone are not good evidence of a therapy's ultimate effects. In our therapy summaries, we list clinical evidence first, and then we include lab and animal evidence for further insights. When no clinical evidence is available, lab and animal evidence is offered, but we do not consider it strong evidence.

This handbook focuses on therapies with clinical evidence of effects in prostate cancer. However, we also include therapies with particularly promising animal evidence. These are the Group 5 therapies in each category.



Treating the Cancer

Working against cancer growth or spread, improving survival, or working with other treatments or therapies to improve their anticancer action

Effective treatment begins with an accurate diagnosis. According to a 2019 Cochrane review and meta-analysis, MRI (magnetic resonance imaging) pathway is better than systematic biopsies in making a correct diagnosis of clinically important prostate cancer and reducing redundant biopsies and the detection of unimportant cancers substantially.⁵²

Conventional Prostate Cancer Therapies

Not that long ago, radical surgery and/or radiation therapy were standard care after a prostate cancer diagnosis. Current approaches, even within conventional care, are much less aggressive. Mark Scholz, MD, and Ralph Blum explain that radical surgery and/or radiation therapy may or may not be the best approach for you. Whichever prostate cancer treatment specialist you see, you will most likely get a good explanation of their preferred therapy, but many will not be able to adequately tell you about other options.⁵³

Conventional prostate cancer therapies may provide alternatives to more invasive treatments and may come with fewer side effects that affect your long-term quality of life:

- Ablating the prostate gland rather than surgically removing it. Ablation involves using small needle probes placed into the prostate or high-frequency ultrasound energy to cause temperature changes that kill the cancer cells.
- Radiation therapy, such as hypofractionated intensity-modulated radiation therapy (IMRT), that require fewer treatments with comparable or better outcomes to the more common Fractionated IMRT.⁵⁴
- MRI-guided transurethral ultrasound ablation (TULSA) is a minimally-invasive procedure being investigated for safety and effectiveness.⁵⁵ The manufacturer provides a Treatment Locator page.

Not all those with prostate cancer will be good candidates for these therapies. Getting the diagnosis right and considering all your options is essential to success:

- With the correct diagnosis, further tests can predict if your cancer is likely to grow and spread, allowing you to hone in on the treatment options specific to you.
- Other additional tests, both novel and standard, can provide information about your cancer cells or your terrain, which hosts the cancer cells.

A starting place for the science of conventional therapies:

- National Cancer Institute:
 - About Cancer, www.cancer.gov/about-cancer
 - Prostate Cancer—Patient Version, www.cancer.gov/types/prostate
 - Prostate Cancer—Health Professional Version,
 - www.cancer.gov/types/prostate/hp
- Cancer.net: Prostate Cancer, https://www.cancer.net/cancer-types/prostatecancer

Predicting Treatment Outcomes

Predict Prostate is an online prognostic tool from the University of Cambridge. It uses an individualized prognostic model for men newly diagnosed with nonmetastatic prostate cancer to compare the outcomes from conservative management (or monitoring) with radical treatment (surgery or radiotherapy). This tool is endorsed by the UK National Health Service (NHS) and Public Health England. Online at prostate.predict.nhs.uk/

Natural Products

Group 3: Limited clinical evidence of efficacy but good safety, used in leading	
integrative programs	

Therapy	Notes	
Green tea extract	 Reduced serum levels of PSA, HGF, and VEGF in men with prostate cancer, with no elevation of liver enzymes in men with positive prostate biopsies and scheduled for radical prostatectomy⁵⁶ Trend toward beneficial changes in serum prostate-specific antigen, serum insulin-like growth factor axis, and oxidative DNA damage in blood leukocytes, plus a decrease in Gleason score from biopsy to surgery in men with prostate cancer scheduled to undergo radical prostatectomy⁵⁷ 	

	 No or minimal clinical activity against hormone refractory prostate cancer in a small study⁵⁸ Notable preclinical evidence: regulated androgen action in cell and animal studies⁵⁹ Used in these programs and protocols: Alschuler & Gazella complementary approaches Block program Lemole, Mehta & McKee protocols
Isoflavones, including soy supplements and red clover Benefits of consuming soy foods are discussed above in Eating Well.	 Supplementation with genistein and other soy isoflavones lowers⁵⁰ or stabilizes⁶¹ PSA levels in men with prostate cancer. Red clover is associated in studies with decreased PSA levels, but with a concern that this could mask the development of prostate cancer.⁶² Anticancer effects with genistein supplementation include changes in expression of genes involved in developmental processes, stem cell markers, proliferation and transcriptional regulation.⁶³ Decreased serum sex hormone levels but not androgen receptor expression in a small pilot study⁶⁴ Notable preclinical evidence: Decreased tumor volume in animals with genistein combined with AG1024⁶⁵ Reduced metastasis in animal studies⁶⁶ In high concentrations, pure genistein induced metastasis in mouse xenograft models, although the addition of diadzein (in soybeans and various products) may prevent this response.⁶⁷ Soy and genistein are used in these programs and protocols: Block program McKinney protocols. Ornish Lifestyle Medicine
Lycopene Benefits of consuming tomatoes and other foods high in lycopene are discussed above in Eating Well.	 Reduced PSA levels and other markers of prostate cancer progression in men with prostate cancer⁶⁸ Stabilized serum PSA level in men with rising serum PSA following local therapy or while on hormone therapy, both alone or in combination with soy isoflavones⁶⁹ Notable preclinical evidence: Enhanced antitumor efficacy of the chemotherapy drug docetaxel against prostate cancer in animal studies.⁷⁰ Down-regulation of androgen metabolism and signaling in prostate cancer in preclinical studies⁷¹ Used in these programs and protocols:

	 Block program Chang strategies for cancer risk reduction McKinney protocols Used in traditional Chinese medicine
Modified citrus pectin	 Significantly increased prostate specific antigen doubling time in patients with recurrent prostate cancer in a small study⁷² Stabilized disease in some patients in a pilot study⁷³ Notable preclinical evidence: Reduced metastasis in cell studies in combination with a polybotanical compounds for prostate health, ProstaCaid™⁷⁴ Sensitized prostate cancer cells to radiotherapy in cell studies⁷⁵ Used in these programs and protocols: Alschuler & Gazella complementary approaches McKinney protocols
Omega-3 fatty acid supplements containing DHA and EPA Benefits of consuming foods high in omega-3s are discussed above in Eating Well.	 When combined with a low-fat diet, omega-3s led to smaller prostates (both benign and malignant components), lower proliferation index, and other anticancer effects.⁷⁶ Increased resistance to chemotherapy; not recommended on the days surrounding chemotherapy⁷⁷ No effects found with EPA supplements used alone⁷⁸ Used in these programs and protocols: Alschuler & Gazella complementary approaches Lemole, Mehta & McKee protocol McKinney protocols
Pomegranate fruit and extract	 Preliminary evidence that supplementation with pomegranate extract lowers PSA levels in men with prostate cancer⁷⁹ Prolonged PSA doubling time⁸⁰ Pomegranate juice and extract were safe but did not significantly improve outcomes in men undergoing radical prostatectomy,⁸¹ in men following primary therapy¹⁶ or in biochemical recurrence patients,⁸² although a subset of BCR patients with the MnSOD AA genotype responded positively in these last two studies. Used in these programs and protocols: Alschuler & Gazella complementary approaches McKinney protocols

Sulforaphane Benefits of consuming cruciferous vegetables high in sulforaphane are discussed above in Eating Well.	 Lowers PSA levels in men with prostate cancer,⁸³ with more modest reductions in recurrent cancer⁸⁴ Used in the McKinney protocols
Tetrathiomolybdate (TM) and other copper chelators	 Slower PSA progression in a small clinical trial of TM, but with uncertain clinical significance⁸⁵ Copper depletion with TM did not delay disease progression in a small clinical trial of patients with asymptomatic metastatic hormone-refractory prostate cancer.⁸⁶ Notable preclinical evidence: anticancer effects in prostate cancer cells from pyrrolidine dithiocarbamate (PDTC) but not TM⁸⁷ Used in the Block program
Vitamin C	 Intravenous vitamin C modulated inflammation correlated with decreases in tumor marker levels in a pilot study⁸⁸ No benefit found from intravenous vitamin C in an uncontrolled pilot study of patients with chemotherapy-naïve, metastatic, castration-resistant prostate cancer⁸⁹ Used in these programs and protocols: McKinney protocols (high-dose vitamin C) Ornish Lifestyle Medicine
Zyflamend: mixture of rosemary, turmeric, ginger, holy basil, green tea, hu zhang, chinese goldthread, barberry, oregano, baikal skullcap	 Significant improvements in PSA and biopsy markers, with no reported serious adverse events or toxicities in small clinical trials; considered "promising"⁹⁰ Used in the McKinney protocols

Group 4: Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Therapy	Notes
Active hemicellulose compound (AHCC) or	• One case study showed a positive PSA response to active hemicellulose compound, ⁹¹ but a study of

active hexose correlated compound	active hexose correlated compound showed no effect. ⁹²
Artemisinin	 Case study of tumor remission after short-term bicalitumide treatment; seven months later, the tumor developed resistance to artemisia⁹³ Used in traditional Chinese medicine
Combination therapies Benefits of consuming foods containing many of these nutrients are discussed above in Eating Well.	 Curcumin and soy isoflavones Decreased PSA levels in patients with PSA of 10 or higher⁹⁴ Hydroxycitrate, lipoic acid and anti-androgen Dramatic fall (90 percent) in prostate-specific antigen in a patient with advanced prostate cancer resistant to hormonotherapy⁹⁵ Supplement consisting of soy isoflavones, lycopene, silymarin (milk thistle) and antioxidants Improved measures of PSA⁹⁶ Milk thistle (silymarin) and selenium Reduced two markers of lipid metabolism known to be associated with prostate cancer progression in a small study⁹⁷ See more about selenium in Reducing Risk Group 6 below. Selenium, omega-3 fatty acids and soy isoflavones added to a dietary intervention including tomato products, grape/pomegranate juice and green/black tea Lower PSA in patients with non-metastatic prostate cancer after three weeks in a small trial¹⁷ See more about selenium in Reducing Risk Group 6 below.
Cranberry juice or extract	• Lowered serum PSA prior to surgery ⁹⁸
Hydroxycitrate, found in the Garcinia gummi- gutta (tamarind) fruit	 One case of dramatic improvement in PSA in advanced prostate cancer resistant to hormonotherapy when used in combination with lipoic acid and anti-androgen⁹⁵ Associated with liver toxicity,⁹⁹ and possibly mania¹⁰⁰ Used in McKinney protocols Used in Ayurveda
Supplement blends: • Apatone® • Pomi-T	 Apatone®: vitamin C and vitamin K₃ Decreased, PSA velocity and increased PSA doubling time in patients who had failed standard therapy.¹⁰¹ Pomi-T: pomegranate seed, green tea, broccoli and turmeric

 Prostate Health Cocktail (PHC) Block program custom blend 	 Reduced rise in PSA and and increase in the number of men with stable PSA at six months¹⁰² Prostate Health Cocktail (PHC): vitamin D₃ (cholecalciferol) 400 IU, vitamin E (alpha tocopherol) 400 IU, selenium (L-selenomethionine) 200 mcg, green tea extract (epigallocatechin) 400 mg, saw palmetto berry (permixon) 320 mg, soy isoflavones (genistein, daidzein) 20 mg each, lycopene 10 mg Decrease prostate specific antigen (PSA) in one-third of patients without reducing male sex hormones (testosterone and dihydrotestosterone)¹⁰³ Vitamin and mineral supplementation from concentrated food or supplement sources: vitamin C, B vitamins (1, 2, 3, 5, 6, 9, 12), vitamin A, vitamin D, vitamin E, ascorbyl palmitate (absorbable vitamin C), calcium ascorbate, magnesium ascorbate, zinc ascorbate or glycinate, selenium, chromium picolinate and iodine Caution notes: Vitamin B₉ (folate / folic acid) and possibly B₁₂ may fuel prostate cancer risk or progression;¹⁰⁴ advised not to use in advanced prostate cancer Unless diagnosed with an iron or copper deficiency, do not supplement with iron or copper; iron promotes cancer growth and copper promotes angiogenesis (creation of blood vessels to supply tumors) Used in the Block program See concerns regarding vitamin E in Group 6 below.
Vitamin D3	 Serum levels: Better prognosis with medium or high serum levels compared with low levels (<50 nmol 1⁻¹),¹⁰⁵ with a stronger effect in patients receiving hormone therapy¹⁰⁶ Higher mortality with both low and very high serum levels¹⁰⁷ Reduced tumor proliferation with higher serum 1,25 dihydroxyvitamin D levels, but not serum 25 hydroxyvitamin D levels, in a small study¹⁰⁸ Very low levels in younger men were associated with more aggressive prostate cancer¹⁰⁹

 Reduced tumor tissue inflammation and progression of low-grade prostate cancer in pilot studies¹¹⁰ Modestly lowered both PSA and serum PTH before radical prostatectomy¹¹¹ Decreased positive cores in some patients with low-risk prostate cancer under active surveillance¹¹² Reduced PSA levels in patients with asymptomatic, PSA-progression of prostate cancer with use of vitamin D₂ (ergocalciferol)¹¹³ Anticancer effects including enhanced activity of docetaxel and improved PSA, measurable disease response rates and time to progression and survival in several small clinical studies but no improvements in others¹¹⁴ Notable preclinical evidence: In a mouse study, both calcitriol and another form of vitamin D slowed androgen-stimulated tumor progression initially, but prolonged treatment with calcitriol resulted in development of a resistant and more aggressive disease associated with increased distant organ metastasis.¹¹⁵ Used in these programs and protocols: Alschuler & Gazella complementary approaches Chang strategies
 Alschuler & Gazella complementary approaches Chang strategies McKinney protocols See Commentary below. High levels can lead to hypercalcemia¹¹⁶

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Therapy	Notes
Black cohosh	• Inhibited tumor development, proliferation and composition in mice ¹¹⁷
Boswellia	 Reduced proliferation and promoted cell death (apoptosis) and antitumorigenic effects in chemoresistant prostate cancer cells¹¹⁸ Constituents inhibited the growth of docetaxel- resistant prostate cancer cells in lab and animal studies.¹¹⁹
Curcumin	• Decreased cell proliferation, increased cell death (apoptosis), and reduced angiogenesis (creation of

Benefits of consuming turmeric are discussed above in Eating Well.	 new blood vessels to supply tumors) in mice and in human cells grafted into mice¹²⁰ Suppressed human prostate cancer stem cell proliferation and invasion in cell studies¹²¹ for both androgen-sensitive and androgen-independent prostate cancer cells¹²² Sensitized prostate cancer cells to chermotherapy drugs and radiation in animal and cell studies, while protecting normal cells¹²³ Inhibiting bone metastatic processes¹²⁴
Ginger	 Cytotoxic against prostate cancer cells grafted into mice¹²⁵
Ginseng	 Extracts show anticancer effects including induced cell death (apoptosis) and reduced prostate cancer cell viability in animal and lab studies¹²⁶ Used in traditional Chinese medicine and Ayurveda
Indole-3-carbinol (I3C) Benefits of consuming cruciferous vegetables high in I3C are discussed above in Eating Well.	• Reactivated PTEN, a potent tumor suppressor gene, in mice, leading to potent suppression of tumorigenesis ¹²⁷
Inositol hexaphosphate (IP-6)	 Inhibited growth and angiogenesis (creation of blood vessels to supply tumors) of prostate cancer in mice¹²⁸
Medicinal mushrooms	 Treatment with PSP extract from turkey tail mushrooms sensitized cancer cells toward γ-T3-induced cytotoxicity, and the combination of PSP and γ-T3 treatments significantly reduced the growth of prostate tumor in animals.¹²⁹ Reishi mushrooms inhibited the testosterone-induced growth of the ventral prostate in castrated rats,¹³⁰ induced growth arrest and cell death (apoptosis) in prostate cancer cell lines¹³¹ and suppressed cell adhesion and migration of highly invasive prostate cancer cells¹³² Reduced tumor growth with white button mushroom extract in mice¹³³
Melatonin	 Inhibited prostate cancer tumorigenesis and markers with oral administration of melatonin in mice¹³⁴ Mice with human prostate cancer cell xenografts were injected with blood from human volunteers either rich

	or deficient in nocturnal melatonin. Melatonin-rich blood suppressed prostate cancer signal transduction, metabolic and growth activity, while blood from humans exposed to light at night markedly stimulated human prostate cancer growth, signal transduction and metabolic activity. ¹³⁵
Milk thistle	 Inhibited tumor growth,¹³⁶ through reduced vascularity in animals in one study¹³⁷ Inhibited growth of advanced human prostate cancer cells in animals through anti-proliferative, anti-angiogenic and other anticancer effects, especially with isosilybin B¹³⁸ Used in these programs and protocols: Alschuler & Gazella complementary approaches Block program Lemole, Mehta & McKee protocol McKinney protocols Used in traditional Chinese medicine and Ayurveda
Quercetin, ellagic acid and other flavanols and flavanoids including equol, luteolin, DHC, and fisetin	 Inhibited prostate cancer growth in animal studies¹³⁹ Resensitized enzalutamide-resistant prostate cancer cells to enzalutamide treatment in mouse xenografts¹⁴⁰
Saw palmetto	• Lab and animal evidence of reduced proliferation of prostate cancer cells ¹⁴¹

Other therapies with preclinical evidence only for treating the cancer

- African cherry
- Alpha-lipoic acid
- Anthocyanidins (delphinidin)
- Ashwagandha
- Boron
- Cannabinoids
- Coenzyme Q10
- Eugenol
- Garlic
- Ginkgo biloba
- Glucosinolates and isothiocyantes diindolymethane (DIM), sulforaphane
- Grape seed extract
- Lycopodine
- Magnolia bark (Honokiol)
- ProstaCaid[™]

- Red yeast riceResveratrol
- Scutellaria barbata
- Ursodiol (Urso)
- Vitamin K
- Vitex agnus-castus extract

Group 6: Evidence of no efficacy or may be dangerous

Therapy	Notes
Beta carotene	 Evidence of no benefit but also no harm during radiation therapy¹⁴²
Combination therapies Benefits of consuming green tea or tomatoes and other foods high in lycopene are discussed above in Eating Well.	 Lycopene, green tea catechins and selenium Higher incidence of prostate cancer at rebiopsy and expression of microRNAs implicated in prostate cancer progression¹⁴³ See more about selenium in Reducing Risk Group 6 below.
DHEA (dehydroepiandrosterone)	 Can raise levels of sex hormones¹⁴⁴ Recommendation against use the McKinney protocols, and against use of plant sterols and sterolines because they can raise DHEA levels
Qilan capsules (consisting of astragalus, fenugreek, gynostremma, pentaphyllan and smilaz glabra)	• No effects found ⁷⁸
Polyphenol E	• No effects found ⁷⁸
Polysaccharide/oligosaccharide complex obtained from a shiitake mushroom extract (SME)	• No effects found in clinical studies ⁹²
Vitamin E supplements	 Serum levels: Improved prostate cancer survival in adult male smokers with higher serum alphatocopherol at baseline¹⁴⁵ Supplements: Increased risk of prostate cancer among healthy men in a large study taking synthetic all rac-alpha-tocopheryl acetate supplements,¹⁴⁶ limited to those with lower

baseline selenium levels, with indications of differences by genetic types ¹⁴⁷
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Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Therapy	Notes
Chronomodulated therapy	 Increased toxicities and biochemical failure rates seen with evening radiation treatment in prostate cancer patients (indicating that treatment is better at other times); treatment during business hours is the standard of care, but late afternoon treatments may be less optimal than treatment earlier in the day¹⁴⁸ No response with hormone refractory metastatic prostate cancer treated with circadian-timed FUDR chemotherapy¹⁴⁹

Group 2: Good clinical evidence of efficacy & safety, limited access

Some may require a prescription, for example.

Therapy	Notes
Bisphosphonates	 Improved survival with sodium clodronate but not zoledronic acid when used with docetaxel in men with metastatic disease, but no improvement with locally advanced disease¹⁵⁰ Probably reduced the number of participants with disease progression¹⁵¹ Requires a prescription from a licensed physician
Metformin	 Decreased overall and prostate cancer-specific mortality among older men with both diabetes and prostate cancer. The longer the treatment with metformin, the greater the decrease in mortality.¹⁵² A systematic review and meta-analysis concluded that metformin may be a useful adjuvant (supplemental therapy in prostate cancer patients receiving radical radiotherapy.¹⁵³ Significant reduction in BCR (biochemical recurrence) in prostate cancer, but not in all-cause mortality.¹⁵⁴ Improved PSA levels without reported serious adverse events or toxicities⁹⁰ Requires a prescription from a licensed physician Used in McKinney protocols, monitoring vitamin B₁₂ status

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Therapy	Notes
Low-dose naltrexone (LDN)	 Anecdotal reports of LDN associated with remission of prostate cancer untreated by prior hormone-blocking therapy¹⁵⁵ Requires a prescription from a licensed physician Used in these programs and protocols: Block program McKinney protocols

Group 4: Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Therapy	Notes
Aspirin, COX-2 inhibitors and other nonsteroidal anti- inflammatory drugs (NSAIDs)	 Longer overall survival but not prostate cancer-specific survival with aspirin use in some analyses¹⁵⁶ but not all¹⁵⁷ Reduced incidence of lethal cancers (metastatic or fatal) with aspirin use¹⁵⁸ Increased disease-free survival in men of African-American descent with aspirin use¹⁵⁹ No benefit from post-diagnostic aspirin use in a prospective study¹⁶⁰ Longer PSA doubling time in a small clinical trial when used with vitamin D in men with recurrent cancer¹⁶¹ Reduced metastasis¹⁶² Can have serious, even life-threatening side effects; use only under medical supervision Used in these programs and protocols: Block program Celebrex used in Chang strategies Low-dose ("baby") aspirin used in Chang strategies to decrease risk of cardiovascular events and clots which can be caused by Celebrex and Chinese herbs
Cryotherapy	• Rate of disease recurrence varied between 13.2 percent and 26 percent with high rates of maintained urinary continence and sexual potency following treatment; bowel habits and sexual function after four years were comparable to active holistic surveillance patients ¹⁶³

	• Inferior outcomes compared to brachytherapy in low- to intermediate-risk prostate cancer ¹⁶⁴
Gamma-delta T-cell immunotherapy (amino- bisphosphonates+IL-2)	• Superior objective responses to current second-line therapies for advanced prostate cancer in small clinical trials ¹⁶⁵
Gossypol	 Extended overall survival in high-risk metastatic castration-resistant prostate cancer patients, but not other patients¹⁶⁶ Decreased PSA levels in a small clinical trial, with adverse side effects at higher doses including fatigue, nausea/vomiting, diarrhea and ileus (a painful obstruction of the ileum or other part of the intestine)¹⁶⁷ Failed to reduce PSA to target levels when combined with androgen deprivation therapy, and with serious adverse events in 12 of 55 participants¹⁶⁸ Notable preclinical evidence: Enhanced the antitumor activity of X-ray irradiation in mice, leading to tumor regression¹⁶⁹ Apogossypol, a gossypol derivative, inhibited tumor growth in a dosedependent manner with reduced toxicity in animals compared with gossypol.¹⁷⁰
Itraconazole	 Findings from a 2018 phase 2 clinical trial:¹⁷¹ Modulated serum PSA levels modestly without lowering serum testosterone Risk of toxicities associated with mineralocorticoid excess Requires a prescription from a licensed physician
Statins	 Improved prostate cancer-specific survival, especially in advanced cancer and/or with radiation therapy.¹⁷² Decreased cancer-specific and all-cause mortality with use¹⁷³ Sensitized cancer cells to radiation and may improve prostate cancer-specific survival with radiotherapy¹⁷⁴ Associated with serious side effects including permanent muscle damage, increased incidence of diabetes and impaired cognitive function; their potential benefits in prostate cancer must be weighed against the risk, and they should be discontinued promptly if serious side effects occur Requires a prescription from a licensed physician Used in these programs and protocols:

• Chang strategies

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Therapy	Notes
Diclofenac	 Inhibited growth and reduced tumor weight and volume in animals¹⁷⁵
Noscapine	 Limited tumour growth and lymphatic metastasis in mice, with stronger effects if used prophylactically¹⁷⁶ Requires a prescription from a licensed physician
Propranolol and other beta blockers	 Blocked the norepinephrine-induced migratory activity of cancer cells in animal studies¹⁷⁷ Beta blockers, including those of the non-selective type, were not associated with a decreased risk of mortality, either from prostate cancer or from all causes.¹⁷⁸ Requires a prescription from a licensed physician

Group 6: Evidence of no efficacy or may be dangerous

Therapy	Notes
Dipyridamole (Persantine)	• No meaningful improvement in response to chemotherapy in small clinical trials ¹⁷⁹

Diets and Metabolic Approaches

- Ketogenic diet
 - Animal studies show a positive effect slowing tumor growth in prostate cancer, but not improving survival, with the ketogenic diet compared to western diet.¹⁸⁰ Clinical trials are currently in progress.
- Macrobiotic diet
 - Anthony Sattilaro, MD, diagnosed with metastatic prostate cancer, experienced complete resolution of his bone lesions at one and four years after diagnosis. Reviews have not found sufficient evidence of cancertreating effects to recommend this diet.¹⁸¹

Therapies using Heat, Sound, Light or Cutting-edge Radiotherapy

- Hyperthermia
 - Local and regional hyperthermia is being used in Europe and the US; it may be combined with radiation therapy in treating prostate cancer. No evidence of effects has been published to date.



Managing Side Effects and Promoting Wellness

Managing or relieving side effects or symptoms, reducing treatment toxicity, supporting quality of life or promoting general well-being

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Therapy	Notes
Cranberry	 Reduced incidence of urinary tract infections in men during or
juice or	after radiotherapy for prostate cancer ¹⁸² Reduced incidence of cystitis in men receiving radiation therapy
extract	for prostate cancer (limited evidence) ¹⁸³

Group 2: Good clinical evidence of efficacy & safety, limited access

Some may require a prescription, for example.

Therapy	Notes
Medical cannabis and cannabinoids	 A 2018 review from the National Academy of Sciences, Engineering and Medicine drew these conclusions:¹⁸⁴ Effective for treating pain in adults and chemotherapy- induced nausea and vomiting (Conclusive or substantial evidence) Improved secondary sleep disturbances (moderate evidence) Insufficient evidence of improved appetite or anxiety Access varies by country or US state, with moderately easy access in some areas and no or very limited legal access in others
Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Therapy	Notes	
Aged garlic extract	 Protected against radiation and chemical exposure, and long-term toxic damage¹⁸⁵ Used in the Alschuler & Gazella complementary approaches to relieve radiation enteritis 	
Magnesium	 Conflicting evidence of reduced incidence of hot flashes, but not involving prostate cancer survivors¹⁸⁶ Evidence of no effect on weight loss in a small randomized controlled trial of patients with testicular cancer, while also creating a "metallic taste" side effect¹⁸⁷ Used in the McKinney protocols for hot flashes 	
Melatonin and circadian activity/sleep cycle integration	 Decreased pain scores and tramadol consumption, as well as enhanced sleep quality, sedation scores and subjective analgesic efficacy during the postoperative period in patients undergoing elective prostatectomy¹⁸⁸ Patients with advanced lung cancer suffering greater circadian activity/sleep cycle disruption suffer greater interference with function, greater anxiety and depression, poorer nighttime sleep, greater daytime fatigue, and poorer quality of life than comparable patients who maintain good circadian integration.¹⁸⁹ Melatonin is used in these programs and protocols: Alschuler & Gazella complementary approaches McKinney protocols 	
Mistletoe (Viscum album extract)	 Reviews of studies found improved quality of life among patients with unspecified cancers. One study listed benefits in coping, fatigue, sleep, exhaustion, energy, nausea, vomiting, appetite, depression, anxiety, ability to work, and emotional and functional well-being and—less consistently—in regard to pain, diarrhea, general performance, and other side effects of conventional treatments.¹⁹⁰ Used in McKinney protocols Used in traditional Chinese medicine 	
Omega-3 fatty acid supplements containing DHA and EPA	 Ameliorated muscle loss and myosteatosis (the presence of intermuscular and intramuscular adipose tissue) in clinical studies¹⁹¹ Used in the Block program to reduce radiation toxicity and relieve radiation enteritis 	
Probiotics	 May reduce acute radiotherapy-related diarrhea¹⁹² Used in the Block program to reduce radiation enteritis 	

Pycnogenol® pine bark extract	 A small clinical study found these effects in cancer (but not prostate cancer) patients receiving radiotherapy or chemotherapy:¹⁹³ Decreased incidence of nausea/vomiting, diarrhea, edema, weakness and weight loss Reduced cognitive impairment, cardiotoxicity and neutropenia Reduced need for medication to address side effects Fewer days of hospitalisation Used in the Block program to relieve radiation enteritis
Three sengs decoction (ren shen yang rong tang)	 Reduced moderate to severe fatigue in non-anemic cancer survivors in a small clinical study¹⁹⁴ Used in the Block program to reduce radiation toxicity Used in traditional Chinese medicine
Vitamin A (retinol)	 Reduced oral mucositis in a small group of patients¹⁹⁵ (not common in prostate cancer, but possible with some treatments) Reduced radiation proctopathy with retinol palmitate¹⁵² Used in the Block program to relieve radiation enteritis
Vitamin C	 Intravenous vitamin C alleviated cancer- and chemotherapy- related symptoms, including fatigue, insomnia, loss of appetite, nausea, and pain, and also improved physical, role, cognitive, emotional, and social functioning, as well as overall health¹⁹⁶ Used in the Block program to relieve radiation toxicity

Group 4: Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Therapy	Notes
Aloe vera	• Improved some symptoms of acute radiation proctitis induced by radiotherapy of pelvic area: diarrhea, fecal urgency and impact on lifestyle, but no improvement in hemorrhage and abdominal/rectal pain in a small clinical trial ¹⁹⁷
Ashwagandha	• Improved fatigue, vigor, and sexual and psychological well- being in a small study of overweight men aged 40-70 years with mild fatigue (but not cancer patients); also increased dehydroepiandrosterone (DHEA) and testosterone levels, which could be a concern with prostate cancer ¹⁹⁸
Curcumin	 Much milder urinary symptoms in patients undergoing external beam radiotherapy¹⁹⁹

	 Protected intestinal mucosa from radiotherapy-induced damage in rats fed curcumin²⁰⁰ No interference in radiation treatment outcomes after three months²⁰¹
Green tea extract	• Reduced lower urinary tract symptoms in men with high-grade prostate intraepithelial neoplasia ²⁰²
Modified citrus pectin	• Improved physical functioning, role functioning, social functioning, global health status, fatigue, pain, difficult or labored breathing, insomnia and appetite loss compared to the baseline in some patients in a pilot study ⁷³
Saw palmetto	 Reduced lower urinary tract symptoms during radiation therapy²⁰³ Used in traditional Chinese medicine and Ayurveda
Soy isoflavones	 Reduced urinary, bowel, and sexual adverse symptoms induced by radiation therapy²⁰⁴
Supplement blends	 Vitamin and mineral supplementation from concentrated food or supplement sources: vitamin C, B vitamins (1, 2, 3, 5, 6, 9, 12), vitamin A, vitamin D, vitamin E, ascorbyl palmitate (absorbable vitamin C), calcium ascorbate, magnesium ascorbate, zinc ascorbate or glycinate, selenium, chromium picolinate and iodine Caution notes:²⁰⁵ Vitamin B₉ (folate/folic acid) and possibly B₁₂ may fuel prostate cancer progression;¹⁰⁴ advised not to use in advanced prostate cancer Unless diagnosed with an iron or copper deficiency, do not supplement with iron or copper; iron promotes cancer growth and copper promotes angiogenesis See more about selenium in Reducing Risk Group 6 below. Dixentil: 10mg zinc, 500mg galacto-oligosaccharides, 10mg L acidophilus, 10mg L. casei, 1mg vitamin B₁, 1mg vitamin B₂, 1mg vitamin B₆, 10mg nicotinamide Reduced diarrhea incidence and severity including during pelvic radiation treatments²⁰⁶ Milk thistle (silymarin) and selenium Improved quality of life scores in a small study⁹⁷ See more about selenium in Reducing Risk Group 6 below.
Vitamin D	 Improved pain, muscle strength and quality of life in patients with advanced hormone-refractory prostate cancer²⁰⁷ Higher levels led to better response to influenza vaccines in prostate cancer patients.²⁰⁸

	 Serum 25-hydroxyvitamin D concentrations of <35 nmol/L in male and <40 nmol/L in female patient was associated with increased severity of radiation-induced acute proctitis.²⁰⁹ Improved bone health in patients with prostate cancer when used with calcium;²¹⁰ however, a 2012 review and analysis concluded that "at the doses commonly recommended, 500-1,000 mg calcium and 200-500 IU vitamin D per day, men undergoing androgen deprivation lose bone mineral density."²¹¹ The authors note that "high levels of dietary calcium and calcium supplement use are associated with higher risks for cardiovascular disease and advanced prostate cancer", and so higher supplementation cannot currently be recommended for men in treatment for prostate cancer.
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Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Therapy	Notes
Ginkgo biloba	• Inhibited the formation of radiation-induced chromosome- damaging clastogenic factors and ultraviolet light-induced oxidative stress in preclinical studies ²¹²
Grape seed extract	 Ameliorated some of the cytotoxic effects on normal cells/tissues induced by chemo- or radiotherapy in preclinical studies²¹³ Inhibited UV radiation-induced suppression of the immune system in animals²¹⁴
Panax ginseng	 Attenuated irradiation-induced myelosuppression, decreased oxidative stress and normalized increased serum liver enzymes and hepatic protein levels in liver tissue of mice exposed to x-ray radiation²¹⁵ Protected cell lines from ultraviolet radiation²¹⁶ No significant benefit on cancer-related fatigue compared to placebo²¹⁷

Group 6: Evidence of no efficacy or may be dangerous

Therapy	Notes
Black cohosh	 Reduced hot flashes in small studies, although not replicated in large studies, and mostly in studies of women²¹⁸ Used in traditional Chinese medicine
L-glutamine	• Supplements do not prevent radiotherapy-induced diarrhea ¹⁹²

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Therapy	Notes	
Chronomodulated therapy	 Less cisplatin-induced vomiting and subacute renal toxicity in the treatment of urogenital cancer depending on timing of treatment in a small study²¹⁹ (cisplatin may be used in less common types of prostate cancer such as small cell and neuroendocrine) Used in the Block program 	
Hyperbaric oxygen therapy	 Improved scores for radiation injury in late radiation proctopathy²²⁰ Requires a prescription from a licensed physician Mentioned by the Block program to alleviate tissue damage from radiation treatment 	

Mind-Body Approaches

These therapies show benefit for many typical cancer side effects and symptoms:

- Mind-body approaches¹⁰⁷
 - Improvements in overall symptoms of stress, maintained at least 12 months
 - Declined cortisol levels, proinflammatory cytokines, and systolic blood pressure, all correlating with decreased stress and improved quality of life
 - Reduced stress and anxiety
- Tai Chi and qigong
 - No benefit from tai chi for cancer-related fatigue in prostate cancer patients²²¹
 - "Qigong/tai chi during radiation for prostate cancer resulted in superior sleep duration midway through radiation, but this effect was not durable."²²²
- Yoga
 - "Salutogenic (health-promoting) effect in both prostate cancer patients and their caregivers"¹⁰⁷
 - Reduced pre-existing and radiation therapy-related fatigue and urinary and sexual dysfunction in prostate cancer patients²²³

Manipulative and Body-based Methods

- Acupuncture:²²⁴
 - Reduced chemotherapy-induced nausea and vomiting
 - Reduced hot flashes

Energy Therapies

- Reiki:107
 - Improved emotional well-being
 - A positive trend for improvement in anxiety

Bioelectromagnetically Based Therapies

- Transcutaneous electrical nerve stimulation (TENS)
 - Improved postoperative pain²²⁵



Reducing Risk

Reducing the risk of developing cancer or the risk of recurrence

Risk Factors

Risk factors for prostate cancer include these:²²⁶

- Age (increasing risk with aging)
- Race and ethnicity, with men of African-American descent, West African ancestry from the Caribbean and men from South America showing higher incidence and mortality of prostate cancer than white men; Asian men have lower incidence
- Family history of prostate cancer in father or brother
- High serum levels of insulin-like growth factor (IGF-I)
- Sexually transmitted infections
- Obesity
- Smoking
- Alcohol consumption
- Diet (as described above in Eating Well)
- Vasectomy (slightly increased relative risk in some studies)
- Diabetes (conflicting results across studies)
- Environmental exposures as described above in Creating a Healing Environment

A meta-analysis of eight studies found a 24 percent increased risk of prostate cancer with night-shift work, although the authors of an assessment considered the data inconclusive due to high variability among studies and poor study quality.²²⁷ Separate studies of the association between artificial light at night (LAN) and incidence of several cancers "found a significant positive association between population exposure to LAN and incidence rates of prostate cancer, but no such association with lung cancer or colon cancer."²²⁸ Researchers speculate that reduced melatonin production may contribute to the increased risk, but sleep disruption (which is also influenced by melatonin production) and other factors are also potential contributors.

A small study found an association between use of the beta blocker metoprolol and higher risk of metastatic prostate cancer.²²⁹ Until that association is confirmed in a larger study, BCCT does not consider it a concern.

Conventional Therapies

In a large study of associations between testosterone replacement therapy (TRT) and risk of prostate cancer, use was significantly associated with more favorable-risk prostate cancer and lower risk of aggressive prostate cancer.²³⁰ This is considered a surprising find by many oncologists, for conventional treatment is to reduce testosterone.

A 2008 study found that patients who received general anesthesia combined with epidural analgesia had a 57 percent lower risk of cancer recurrence than patients who had general anesthesia and postoperative opioids.²³¹

A 2019 retrospective study from Japan suggests that patients with localized prostate cancer treated with carbon ion radiotherapy appear to have a lower risk of subsequent primary cancers than those treated with photon radiotherapy.²³² Access to carbon ion radiotherapy in the United States has been limited to clinical trials, although the National Cancer Institute has announced a goal to create a carbon therapy instrument and treatment center in the US.²³³

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Therapy	Notes	
Grape seed extract	• Reduced risk of prostate cancer ²³⁴	
Lycopene Benefits of consuming tomatoes and other foods high in lycopene are discussed above in Eating Well.	• Reduced risk of prostate cancer in large meta-analyses with both dietary intake and circulating concentrations of lycopene, but no reduced risk of advanced cancer in one analysis ²³⁵	
Quercetin Benefits of consuming onions, apples and other foods high in quercetin are discussed above in Eating Well.	 Reduced incidence of prostate cancer in epidemiologic studies²³⁶ Notable preclinical evidence: chemopreventive properties in animal studies²³⁷ 	

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Therapy	Notes	
Glucosinolates and isothiocyantes:	 Isothiocyanates are weakly related to	
indole-3-carbinol (I3C),	reduced risk of prostate cancer. ²³⁸	

diindolymethane (DIM), sulforaphane Benefits of consuming cruciferous vegetables high in these nutrients are discussed above in Eating Well.	 Used in these programs and protocols: Block program McKinney protocols
Green tea extract	 Reduced development of prostate tumors in men with high-grade prostate intraepithelial neoplasia (HGPIN)²³⁹ Decreased incidence of prostate cancer plus atypical small acinar proliferation in men with HGPIN without atypical small acinar proliferation at baseline²⁴⁰
Soy isoflavones Benefits of consuming soy foods are discussed above in Eating Well.	 Daidzein concentrations²⁴¹ and genistein intake are both associated with reduced risk.²⁴² Genistein modulated gene changes and epigenetic modifications found in prostate cancer.²⁴³ Soy isoflavones are used in the Block program.
Vitamin E Benefits of consuming foods high in vitamin E are discussed above in Eating Well.	 Serum levels: Progressively higher PSA scores with decreasing serum levels of vitamin E with in a small study²⁴⁴ Decreased risk for developing prostate cancer with higher serum alphatocopherol levels, with a higher association of decreased risk for advanced prostate cancer and a greater association among those taking alphatocopherol supplements²⁴⁵ Reduced total prostate cancer risk and aggressive cancer risk in current smokers with higher alpha-tocopherol or gamma-tocopherol levels, with some evidence of differences among genotypes²⁴⁶ Supplements: Natural vitamin E contains eight tocopherols and tocotrienols, found in different combinations across sources, but vitamin E supplements typically contain only alpha-tocopherol,²⁴⁷ The specific tocopherols used in studies

	 should be noted, for each have different properties and effects.²⁴⁸ Supplementation with higher levels of alpha-tocopherol may affect levels of gamma-tocopherol; the balance and mix of tocopherols may be very important in outcomes.²⁴⁹ Inconsistent evidence: Increased risk or no effect with synthetic all rac alpha-tocopheryl acetate²⁵⁰ Increased risk from alpha-tocopheryl acetate²⁵¹ Reduced risk for both prostate cancer and advanced cancer with alpha-tocopherol in a pooled analysis, but no association with gamma-tocopherol²⁵² Analyses of data propose that risks associated with vitamin E may vary by genotype of patients or by the specific form of vitamin E (alpha-tocopherol versus gamma-tocopherol, for instance)²⁵¹ Recommendation against use by integrative oncologist and BCCT advisor Donald Abrams, MD²⁵³ Used in these programs and protocols: Alschuler & Gazella complementary approaches McKinney protocols (paired with EGCG)
Vitamin K	 Lower risk of prostate cancer with dietary intake of menaquinones (vitamin K₂), but not phylloquinone (vitamin K₁) in a nested case-control study²⁵⁴ Vitamin K₂ is used in these programs and protocols: Lemole, Mehta & McKee protocol McKinney protocols

Group 4: Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Therapy	Notes
Melatonin	 Reduced risk of prostate cancer or advanced stage prostate cancer with high urinary melatonin, melatonin-sulfate levels or a high melatonin-sulfate/cortisol (MT/C) ratio; finding a low MT/C ratio combined with a PSA level exceeding 10□ng/ml showed the greatest potential in detecting prostate cancer and advanced stage prostate cancer.²⁵⁵
Zyflamend: mixture of rosemary, turmeric, ginger, holy basil, green tea, hu zhang, chinese goldthread, barberry, oregano, baikal skullcap	 "Showed promise" in reducing prostate cancer risk²⁵⁶

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Therapy	Notes
Curcumin	Chemopreventive effects in mice ¹²²
Inositol hexaphosphate (IP-6)	• Lab and animal evidence of chemoprotective effects ²⁵⁷
Milk thistle	• Chemoprotective effects in lab and animal studies ²⁵⁸
<i>Pygeum africanum</i> extracts	• Reduced prostate cancer incidence in mice ²⁵⁹
Turkey tail mushroom	• Eliminated prostate cancer stem cells in animal studies ²⁶⁰

Other therapies with preclinical evidence only for reducing risk

- Organosulfur compounds
- Red yeast rice
- Resveratrol

Group 6: Evidence of no efficacy or may be dangerous

Therapy	Notes
Beta carotene, other carotenoids and retinol (vitamin A)	 Regarding beta carotene, retinol and other carotenoids:²⁶² Limited and conflicting evidence of reduced risk Increased risk of prostate cancer with higher circulating retinol concentrations in blood Increased risk of prostate cancer among smokers taking beta carotene supplements
Boron	• Not associated with lower prostate cancer incidence ²⁶³
Calcium supplements Risks of consuming foods high in calcium are discussed above in Eating Well.	• No higher risk of prostate cancer overall, but an increased risk of fatal prostate cancer ²⁶⁴
Coenzyme Q10	 No significant reduced risk of prostate cancer in a large cohort.²⁶¹
Flavonoids, including anthocyanidins	• No effect on reducing risk of prostate cancer onset ²⁶⁵
Folic acid or folate	 Increase in prostate cancer risk in a large case- control study and meta-analyses of epidemiological studies of both folic acid supplementation and blood folate levels²⁶⁶ Recommendation against use in the McKinney protocols
Glucosamine	• No significant reduced risk of prostate cancer ²⁶¹
Omega-3 fatty acid supplements containing DHA and EPA Benefits of consuming foods high in omega-3s are discussed above in Eating Well.	 2018 review conclusions:¹⁰⁷ One study found an <i>increased</i> risk of prostate cancer and of high-grade prostate cancer with the highest blood levels of omega-3 fatty acids, but the study did not assess supplement use. Four grams of supplementation may impair clotting; patients may want to eliminate omega-3 supplements before and immediately after surgery. Conflicting evidence regarding risk: no clear relationship between omega-3s in general or fish-derived omega-3 fatty acids and risk of prostate cancer in some reviews,²⁶⁷ while another small study

	found higher levels of individual components of both omega-6 and omega-3 fatty acids may be associated with higher-grade prostate cancer. ²⁶⁸
Saw palmetto	• Evidence of no reduced risk in a large prospective cohort study ²⁶⁹
Selenium	 Higher blood or nail selenium levels—to a point—are associated with lower risk of prostate cancer in some studies.²⁷⁰ This association may be specific to some genotypes.²⁷¹ However, several studies show either no effect or a trend toward <i>increased</i> prostate cancer risk or more advanced cancer from use of selenium supplements.²⁷² Large studies have found that among men with high levels of selenium at baseline, those taking selenium had a greatly increased risk of high-grade prostate cancer compared to placebo. In one study, men who reported consuming 140+ µg/day of selenium after diagnosis had a 2.6-fold increased risk of prostate cancer mortality.²⁷³
Vitamin A (retinol)	• Evidence of increased risk of prostate cancer ²⁶²
Vitamin C	 No evidence of reduced risk from vitamin C supplements or dietary intake in large studies and reviews²⁷⁴
Vitamin D	 Mixed results across studies and conditions: Increased risk of prostate cancer with higher vitamin D levels: With higher serum levels²⁷⁵ Of aggressive prostate cancer with very high levels of plasma vitamin D (above 70 or 80 nmol/l, depending on the study),²⁷⁶ and more strongly for high-grade disease.²⁷⁷

	 Severe vitamin D deficiency (<12 ng /mL) was associated with increased risk of a prostate cancer diagnosis on biopsy among men of African American descent, and associated with higher Gleason grade and tumor stage in men of both African American and European American descent²⁷⁹ Both low (<50 nmol/L) and high (≥75 nmol/L) vitamin D concentrations were associated with increased risk of prostate cancer, and more strongly for high-grade disease. Authors of this study do not advise supplementation in men with adequate levels.²⁷⁷ High levels can lead to hypercalcemia¹¹⁶ See the Commentary section below.
Zinc	• Decreased zinc levels found in prostate cancer cells is considered an essential early event in prostate oncogenesis. ²⁸⁰ However, a 2016 meta-analysis found no evidence for an association between zinc intake and prostate cancer incidence among men of African- American descent. ²⁸¹

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Group 2: Good clinical evidence of efficacy & safety, limited access

Some may require a prescription, for example.

Therapy	Notes
Metformin	 Significant reduction in BCR (biochemical recurrence) in prostate cancer, but not in all-cause mortality.¹⁵³ Requires a prescription from a licensed physician

Group 4: Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Therapy	Notes
Aspirin, COX-2 inhibitors and other nonsteroidal anti- inflammatory drugs (NSAIDs)	 Reduced risk of developing prostate cancer²⁸² Decreased risk of advanced stage prostate cancer in men of African-American descent¹⁵⁹ Can have serious, even life-threatening side effects; use only under medical supervision See Commentary below.

Finasteride (brand names Proscar, Propecia, and Propecia Pro-Pak) and other 5-alpha reductase inhibitors	 A placebo-controlled, randomized clinical trial found these associations:²⁸³ Reduced prostate cancer risk, with finasteride concentrations affected by variations in genes responsible for altering its metabolism pathway Greater inflammation in benign prostate tissue in those receiving finasteride, but the risk of total and higher-grade cancer was not increased compared to those receiving placebo. Most significant reduction has been seen in low-grade prostate cancer, with a concern that 5-ARIs could potentially increase high-risk prostate cancer and mortality. Although higher mortality has not been seen in follow-up data, 5-ARIs continue to have a black box warning and are not approved for prostate cancer prevention.²⁸⁴ Requires a prescription from a licensed physician Used in Chang strategies
Propranolol	 Reduced risk of prostate cancer²⁸⁵ Requires a prescription from a licensed physician
Statins	 Decreased risk of advanced or aggressive prostate cancer²⁸⁶ Decreased risk of recurrence after radiation therapy²⁸⁷ Decreased risk of biochemical recurrence among patients who received radiation therapy but not radical prostatectomy, and only among men undergoing androgen deprivation therapy²⁸⁸ Increased prostate cancer risk with extended use in obese men Some evidence of reduced risk with statin use,²⁸⁹ but insufficient evidence of benefit to support the use of statins for the primary prevention of prostate cancer²⁹⁰ Associated with serious side effects including permanent muscle damage and impaired cognitive function; their potential benefits in prostate cancer must be weighed against the risk, and they should be discontinued promptly if serious side effects occur Require a prescription from a licensed physician
Vitamin K antagonists, drugs that reduce blood clotting by reducing the action of vitamin K; the most common are coumarins such as warfarin (brand	 Decreased risk of prostate cancer, especially in long-term users, in a meta-analysis²⁹¹ and large population studies²⁹² Requires a prescription from a licensed physician High risk of bleeding if levels are not monitored closely



Optimizing Your Terrain

Creating an environment within your body that does not support cancer development, growth or spread

Natural Products

- Omega-3 fatty acids show some evidence of decreased inflammatory markers in clinical trials.²⁹³
- Intravenous vitamin C modulated inflammation correlated with decreases in tumor marker levels in a pilot study⁸⁸
- Milk thistle (silymarin) and selenium reduced two markers of lipid metabolism known to be associated with prostate cancer progression in a small study.⁹⁷

See more on BCCT's Body Terrain and the Tumor Microenvironment webpage, bcct.ngo/integrative-cancer-care/body-terrain-and-the-tumor-microenvironment

Commentary

In his Grand Rounds Urology lecture, **Aaron Katz, MD**, cites the literature supporting vitamin D's positive effect in reducing disease risk, including prostate cancer. Dr. Katz's practice is to "obtain [baseline] vitamin D levels on all of my [prostate cancer] patients that are on active surveillance, whether it be in the recurrent cases or in primary [cases]. Then. . . restore about 1,000 international units (IUs) of vitamin D, [to] give you just a bump [in blood levels] up of around 10 ng/mL. Most people in the field believe that the therapeutic range is somewhere between 40 and 50 ng/mL. "²⁹⁴

BCCT senior researcher **Laura Pole, RN, MSN, OCNS**: In dosing vitamin D to bring up to therapeutic levels, keep in mind that many clinicians, including BCCT advisor Donald Abrams, MD, feel that doses greater than 4000 IU daily lead to increased risk of calcification of blood vessels. Dr. Katz reports that he has not seen any problems dosing with 5000 IU vitamin D per day for 3 months, then re-checking the vitamin D level. BCCT advises not to take high doses of vitamin D without medical advice and supervision.

BCCT advisor **Keith Block, MD**, says that off-label use of calcitriol, which is the most active form of vitamin D, is of particular interest in prostate cancer.²⁰⁵ Preclinical evidence shows clear benefit and early clinical evidence to date is promising but not yet conclusive.¹¹³ See descriptions of vitamin D in Treating the Cancer, Group 4 and in Reducing Risk, Group 6.

Dr. Block cautions against giving alpha-tocopherol alone, as this may deplete the body of other important components of vitamin E^{205}

Dr. Block prefers to get at the root of inflammation using diet and other non-drug approaches, but in certain situations, he uses Celebrex to block the COX-2 enzyme,

"since the inflammatory chemicals the enzyme spawns play a major role in blocking the effectiveness of chemotherapy and radiation."²⁰⁵ Note that NSAIDs can have serious, even life-threatening side effects; use them only under medical supervision.

Nutrition Advisor **Karen Collins, MS, RDN, CDN, FAND**, American Institute for Cancer Research, July 26, 2019: There are multiple reasons to be cautious about alpha-tocopherol supplements much beyond RDA level. I cannot find evidence of an effect on absorption of tocotrienols and other tocopherols, but it has been known for many years that high levels of alpha-tocopherol intake tend to decrease blood and tissue levels of gamma-tocopherol. (I'm not sure of the reason—perhaps through effects on absorption from the gut, but perhaps on saturation of metabolic enzymes, preferential saturation of carriers within the body, or other mechanisms.)

While there is great interest in the potential of tocopherols and tocotrienols beyond alpha-tocopherol for anticancer effects, these ideas are largely based on in vitro and animal studies. There is a big leap from these kinds of studies to human application, which need to consider dose, bioavailability, potential differences among human populations.

However, it's important to think more broadly about your question, too. Our antioxidant defense network (from exogenous sources and endogenous elements within our body) interact in many ways. So setting any single element high may have ramifications on others. Selenium is one example, which is noted in the references I share below and is still coming up in studies as recently as May.

Perhaps this summary of research and recommendations written for health professionals will be helpful to you: National Institutes of Health Vitamin E: Fact Sheet for Health Professionals. It focuses on alpha-tocopherol, since that is the only form for which we have established recommended intake at this time. The reason I recommend it for your review is that it provides important perspective on potential for excess. Although the Tolerable Upper Intake Levels (set to accompany the RDAs) were developed based on avoidance of hemorrhagic effects, evidence from studies like the SELECT trial show that problems such as increased risk of prostate cancer can occur at levels above the RDA but well below that upper limit. (Remember back in the day when cardiologists were excited to recommend 400 IU to all their heart patients??)

There is also a version written for the public, in case you'd like to link to it in what you're creating: Vitamin E: Fact Sheet for Consumers.

Another reference that may help explain the strong findings about the dangers of antioxidant supplements during cancer treatment: Avoiding Antioxidant-Drug Interactions During Cancer Treatment.

My bottom line: Concern about interactions of alpha-tocopherol supplements with tocotrienols and other tocopherols is only one of several reasons to be concerned about supplementation beyond the RDA, especially well beyond it.

Written by Laura Pole, RN, MSN, OCNS, and Nancy Hepp, MS; most recent update on September 9, 2019. BCCT is grateful for review and feedback on this summary from integrative oncologist and BCCT advisor Donald Abrams, MD, and for the KNOW Oncology resource used in creating this summary.



More Information

Many resources related to integrative approaches to prostate cancer care, conventional approaches, advocacy and support groups and other topics are listed on the BCCT Prostate Cancer page, bcct.ngo/cancers-and-symptoms/cancers/prostate-cancer

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