Breast Cancer

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

October 2019
# Contents

Quick Reference ..................................................................................................... 5  
Key Points .............................................................................................................. 7  
Introduction ........................................................................................................... 8  
   Diagnostic Testing................................................................................................... 9  
Integrative Care in Breast Cancer ........................................................................ 9  
Clinical Practice Guidelines .................................................................................. 10  
   Further Clinical Practice Guidelines ................................................................ 11  
Integrative Programs, Protocols and Medical Systems ......................................... 11  
   Traditional Medicine Systems .......................................................................... 11  
Examples of Integrative Approaches ................................................................... 12  
   The Block Center for Integrative Cancer Treatment (BCICT) .............................. 12  
   Block Center Program Supplements .................................................................. 13  
   Bastyr Integrative Oncology Care: A Naturopathic Oncology Approach .......... 14  
   Bastyr Breast Cancer Study Supplements ...................................................... 15  
   Dr. Kleef: Hyperthermia, Immunology and Integrative Oncology Program ...... 15  
Integrative Therapies in Breast Cancer ................................................................ 16  
   7 Healing Practices: The Foundation ................................................................. 16  
   Dietary Fats: Healthier Choices ......................................................................... 17  
   The Ecology of Breast Cancer .......................................................................... 20  
   Adding Up Benefits ............................................................................................ 21  
   Therapies for Managing Stress ......................................................................... 23  
   Circadian Rhythms and Breast Cancer .............................................................. 26  
   Beyond the 7 Healing Practices: Further Integrative Therapies ....................... 28  
   Cells, Animals and People ................................................................................ 29
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimizing Your Terrain</td>
<td>65</td>
</tr>
<tr>
<td>Natural Products</td>
<td>65</td>
</tr>
<tr>
<td>Off-label, Overlooked and Novel Cancer Approaches (ONCAs)</td>
<td>66</td>
</tr>
<tr>
<td>Breast Cancer and Surgery</td>
<td>66</td>
</tr>
<tr>
<td>Hormone Therapy before Surgery</td>
<td>66</td>
</tr>
<tr>
<td>Breast Reconstruction: Now More Options</td>
<td>66</td>
</tr>
<tr>
<td>Avoiding Complications After Breast Surgery</td>
<td>67</td>
</tr>
<tr>
<td>Post-surgical Pain Management</td>
<td>70</td>
</tr>
<tr>
<td>Dr. Stritter's Approach</td>
<td>72</td>
</tr>
<tr>
<td>Reducing the Risk of Chronic Pain after Mastectomy or Breast...</td>
<td>72</td>
</tr>
<tr>
<td>Infection Response</td>
<td>72</td>
</tr>
<tr>
<td>Recovery and Remission Maintenance</td>
<td>73</td>
</tr>
<tr>
<td>DCIS Treatment</td>
<td>75</td>
</tr>
<tr>
<td>De-escalation of DCIS Treatment</td>
<td>75</td>
</tr>
<tr>
<td>Low-dose Tamoxifen and DCIS</td>
<td>75</td>
</tr>
<tr>
<td>Taking Care of Your Heart: Cardiac Toxicity and Breast Cancer...</td>
<td>76</td>
</tr>
<tr>
<td>“Heart Healthy” Lifestyle Choices</td>
<td>77</td>
</tr>
<tr>
<td>Natural Therapies Protective during Adriamycin/Doxorubicin Treatment</td>
<td>78</td>
</tr>
<tr>
<td>Natural Therapies Protective during Treatment with Herceptin/Trastuzumab, Perjeta/Pertuzumab or Kadcyla/Trastuzumab Emtansine</td>
<td>79</td>
</tr>
<tr>
<td>Commentary</td>
<td>80</td>
</tr>
<tr>
<td>References</td>
<td>83</td>
</tr>
</tbody>
</table>
Breast Cancer

Quick Reference to Integrative Therapies

Items marked (T) are noted as helpful for wellness during tamoxifen treatment. Therapies protective of cardiac tissue during treatment with Adriamycin/doxorubicin are marked (A) and with Herceptin/trastuzumab are marked (H).

7 Healing Practices

Eating Well
- Low-fat, high-fiber, plant-based diet, such as the Mediterranean diet (T) (A) (H)
- Cruciferous vegetables (broccoli, kale, cauliflower, Brussels sprouts, cabbage, bok choy)
- Foods containing omega-3s, especially DHA and EPA (in fish, some seafood, and enhanced eggs and dairy foods)
- Foods containing carotenoids, such as beta-carotene (in sweet potatoes and carrots) and lycopene (in cooked tomatoes and watermelon)
- Green tea (T)
- Whole soy foods (tempeh, miso, edamame, tofu) (T)
- Flaxseed or flax oil

Moving More
- At least 10 MET-hours (metabolic equivalents hours) per week, the equivalent of 3 hours of brisk walking (A) (H)
- A supervised program may lead to higher fitness levels than a self-directed program

Managing Stress
Mind-body approaches:
- Meditation (T) (A)
- Relaxation techniques (T)
- Yoga (T) (A)
- Music therapy
- Tai chi (A)
- Hypnosis
- Expressive art techniques
- CBT stress management (A)

Creating a Healing Environment
- Dark nights
- Bright mornings
- Limit chemical and radiation exposures

Sleeping Well
Natural products:
- Melatonin
- L-theanine (Suntheanin)
- Valerian
- 5-HTP (not with antidepressants)
- Medical cannabis and cannabinoids
Mind-body approaches:
- Cognitive Behavioral Stress Management (CBSM) (A)
- Cognitive Behavioral Therapy for Insomnia (CBT-I)
- Mindfulness meditation (T) (A)
- Tai chi (A)
- Qigong
- Stress reduction practices (A)
- Yoga meditation (A)
- Yoga (T) (A)

Body-Manipulative Therapies
- Acupuncture (T)

Sharing Love and Support
- Support groups
- Supportive-expressive therapy
- CBT social skills training

Also see
- Taking Care of Your Heart section on the BCCT Breast Cancer summary
- Wellness during Tamoxifen Treatment
Natural Products  
*Items in bold are in more than one category.*

<table>
<thead>
<tr>
<th>Treating the Cancer</th>
<th>Managing Side Effects and Promoting Wellness</th>
<th>Optimizing Your Terrain</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Flaxseed</td>
<td>1. Bromelain</td>
<td>1. Agaricales mushrooms</td>
</tr>
<tr>
<td>2. Melatonin (with caution during surgery) (T)</td>
<td>2. CoQ10 (T, A)</td>
<td>2. Curcumin</td>
</tr>
<tr>
<td>5. Vitamin D (T)</td>
<td>5. Medical cannabis and cannabinoids</td>
<td>5. Reishi mushroom</td>
</tr>
<tr>
<td></td>
<td>7. Vitamin D (T)</td>
<td></td>
</tr>
</tbody>
</table>

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

1. Bisphosphonates
2. Propranolol

### Managing Side Effects and Promoting Wellness

1. Bisphosphonates

### Reducing Risk

1. Bisphosphonates
2. Metformin
3. Propranolol

Conventional Therapies

Vaginal moisturizers and vaginal rings supplying low-dose estrogen address sexual discomfort and difficulties.

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

Investigational Therapies

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

<table>
<thead>
<tr>
<th>Treating the Cancer</th>
<th>Managing Side Effects and Promoting Wellness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chronomodulated therapies</td>
<td>1. Agaricales mushrooms</td>
</tr>
<tr>
<td>2. Ginseng</td>
<td>2. Infravenous vitamin C</td>
</tr>
<tr>
<td>3. Maitake mushroom</td>
<td>3. Melatonon</td>
</tr>
<tr>
<td>4. Metformin</td>
<td>4. Propranolol and other beta blockers</td>
</tr>
</tbody>
</table>

### Reducing Risk

1. Agaricales mushrooms
2. Vitamin D supplements (T)
Key Points

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

- Integrative cancer care means skillful choices in both conventional and complementary cancer therapies.
- Breast cancer is many different diseases. Not only will conventional treatment vary from one person to the next, but integrative breast cancer care will vary.
- Getting the diagnosis right is key to selecting your treatment approach. We recommend getting a second pathology reading, especially if the initial report includes any uncertainty, and considering further diagnostic evaluation.
- Pathology reports and other diagnostic testing will help inform your treatment options (see box below), prepare you for possible side effects and guide you in steps to prevent or minimize these effects.
- The American Society of Clinical Oncology has endorsed the breast cancer clinical practice guidelines of the Society of Integrative Oncology, validating integrative breast cancer treatment approaches.
- Available integrative and complementary treatment approaches include integrative protocols and programs and traditional medicine systems.
- We provide examples of different published integrative approaches to advanced breast cancer care.
- 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
- 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 breast cancer.
- We present natural products and off-label, overlooked and novel cancer approaches (ONCAs) in six categories:
  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
   - Surgery involves both benefits and risks. We discuss reducing and managing risks both before and after surgery.
   - People with breast cancer who are undergoing some types of chemotherapy or targeted agents, or who receive radiation therapy to the chest, are at risk for heart damage. We offer guidance on taking care of your heart during breast cancer treatment.
   - Brief information regarding breast reconstruction is provided.

Introduction

Women with breast cancer use integrative therapies more often than any other group of people with cancer.

But despite the widespread use of integrative breast cancer therapies, informed guidance in integrating conventional and complementary breast cancer care is difficult if not impossible to find.

This 40-page summary of science-informed integrative breast cancer care is designed to provide that informed guidance.

Integrative breast cancer care has a remarkable amount to offer you. It can add to your treatment, help with side effects, benefit your quality of life, help you get well again, and reduce your risk of recurrence. Psychologically and spiritually, it can have transformative effects.

Let’s be clear: integrative cancer care means skillful choices in both conventional and complementary cancer therapies.

The very first step is deciding what your goals are. Your goals will guide you in choosing both conventional and complementary therapies. No matter what conventional therapies you choose, our 7 Healing Practices can be beneficial in many ways—physical, emotional, mental and spiritual. They are the foundation to strengthen you for rigorous conventional therapies, reduce side effects, build health and help reduce the risk of recurrence.

Beyond the 7 Healing Practices you will find many specific integrative therapies to explore. Don’t let the number of choices deter you. We’ve arranged them in an easy order to consider, starting with those with the greatest safety, efficacy, and ease of access. Also, don’t overlook our special category of Off-label, Overlooked or Novel Cancer Approaches (we call them ONCAs). They have a lot to offer even if lifestyle changes seem too hard at this point.

I’ve known quite a few 20-year survivors of metastatic breast cancer—and I have known hundreds of women who have far outlived a metastatic prognosis.
We hope to help you live as well as you can for as long as you can with the optimal combination of conventional and complementary therapies. We hope to help you find a way to integrate the therapies that serve you best. That is how the best integrative oncologists do it—and we wish the best for you. Take it slow. Start with the simple things, like our seven healing practices, and move slowly toward the more complex decisions.

Don’t try to take all this in one bite. Take small bites, and come back as you are ready for more.

We do this for you. We hold you in our thoughts and prayers,

Michael Lerner

Diagnostic Testing

Advanced and non-standard diagnostic tests, some specific for breast cancer, are available. These tests can often identify specific therapies that will be most effective. Some require pre-planning for collection and shipping of live tissue samples. See Diagnostic Approaches and De-escalation of DCIS Treatment (below).

Integrative Care in Breast Cancer

Breast cancer is actually many different diseases. Conventional treatments vary. Integrative care should also be individualized. For example, some complementary therapies that enhance immune function in some breast cancers may heighten cancer progression in others.

Getting your diagnosis right is critical to conventional treatment decisions. Unfortunately, accurate reading of pathology reports is often a weak link in cancer treatment, with unacceptably high error rates in some hospitals.

If the diagnosis is wrong, the treatment is often wrong. Many oncologists recommend a second independent reading of your pathology report—preferably from outside your medical center. Some cancer centers do this routinely, especially if they are not certain of the reading.

Further diagnostic tests (see at right), can inform your treatment. They may also help you choose the complementary therapies that may enhance your conventional treatment, help minimize side effects and improve your quality of your life.

You can also prepare yourself for what to expect. You can anticipate side effects and work to minimize them even before treatment starts. Learning what to expect helps you prepare to build your resilience for conventional treatments in the weeks and months to come.
Like conventional therapies, complementary therapies are best explored with a health professional experienced with these therapies. You may want to bring this BCCT Breast Cancer Handbook with you to discuss with your health professional.

Simple complementary and integrative approaches can improve outcomes with breast cancer. More complex approaches can be considered as you get further into your research. We cover both.

**Clinical Practice Guidelines**

The Society for Integrative Oncology (SIO), the leading organization of its kind, has conducted a monumental review of randomized control trials of complementary therapies in breast cancer care. From this review, SIO created integrative care guidelines.

Within one year, the American Society for Clinical Oncology (ASCO) endorsed these guidelines. See the ASCO endorsement in Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline.

The SIO reviewed randomized controlled trials published between 1990 and 2015. Researchers were looking at “the use of integrative therapies for specific clinical indications during and after breast cancer treatment, including anxiety/stress, depression/mood disorders, fatigue, quality of life/physical functioning, chemotherapy-induced nausea and vomiting, lymphedema (swelling), chemotherapy-induced peripheral neuropathy, pain and sleep disturbance.” Recommendations from this review:

- Music therapy, meditation, stress management and yoga for anxiety/stress reduction
- Meditation, relaxation, yoga, massage and music therapy for depression/mood disorders
- Meditation and yoga to improve quality of life
- Acupressure and acupuncture for reducing chemotherapy-induced nausea and vomiting
- A lack of strong evidence supporting the use of ingested dietary supplements or botanical agents as supportive care and/or to manage breast cancer treatment-related side effects

When these guidelines were presented at the 2017 SIO annual meeting, integrative oncologist and BCCT advisor Donald Abrams, MD, pointed out that the guidelines seemed conservative and that experienced integrative oncologists are safely and effectively using evidence-informed therapies that were not included in the SIO recommendations, such as some nutraceuticals and botanicals in advanced breast cancer.

The presenter replied that these guidelines are more conservative because only randomized controlled trials were reviewed, and the guidelines are intended to serve...
the wider audience of oncology clinicians who are not necessarily specialized in integrative oncology care. Dr. Abrams reminded the audience that lack of evidence of effect is not the same as evidence of no effect, and that the safer the therapy that has plausible basis for benefit, the lower the burden of proof.

Further Clinical Practice Guidelines

- National Comprehensive Cancer Network:
  - Professional Guidelines (Login required),
  - Guidelines for Patients:
    - Breast Cancer Early-Stage, www.nccn.org/patients/guidelines/stage_i_ii_breast/files/assets/basic-html/page-1.html

Integrative Programs, Protocols and Medical Systems

Programs and Protocols Specific to Breast Cancer
- Alschuler & Gazella complementary approaches
- Block program
- Chang strategies (case study)
- Cohen & Jefferies risk reduction
- Lemole, Mehta & McKee breast cancer protocol
- MacDonald breast cancer program
- McKinney breast cancer protocol

Traditional Medicine Systems

Traditional Chinese Medicine

Traditional Chinese medicine (TCM) uses botanical and animal products, trace elements, diet and exercise in addition to acupuncture/acupressure, which may be more familiar to many Western patients.

Most controlled studies of TCM in cancer investigate acupuncture. Several Chinese herbals show activity against human breast cancer cell lines in lab and animal evidence, with clinical evidence accumulating more recently. Examples:
• The herb *Scutellaria barbatae* (About Herbs) promotes programmed cell death in patients with advanced metastatic breast cancer in a phase 1 trial.\(^\text{11}\)
• Chinese herbs for breast cancer improved nausea, vomiting and fatigue in a review of randomized trials.\(^\text{12}\)
• Green tea, commonly used in Chinese medicine, is associated with a lower risk of breast cancer and recurrence, with some evidence of therapeutic effects.\(^\text{12}\)

**Ayurvedic Medicine**

According to BCCT advisor Debu Tripathy, MD, no formal studies have evaluated Ayurvedic medicine as a system approach in breast cancer. However, some of the herbs used in Ayurveda—such as curcumin (turmeric) and withafarin A\(^\text{13}\)—have shown activity against breast cancer cell lines in lab studies.\(^\text{10}\)

**Examples of Integrative Approaches**

A number of integrative oncology care programs and clinics employ complementary approaches to enhance conventional treatment and/or minimize side effects. Three programs have published studies of their integrative approaches in caring for those with advanced breast cancer. We provide a description of their research, not as endorsements of their programs, but as examples of different integrative approaches to advanced breast cancer care.

**The Block Center for Integrative Cancer Treatment (BCICT)**

The Block Center, founded by Keith Block, MD, an integrative oncologist and BCCT advisor, offers a comprehensive cancer treatment program combining conventional treatments—often delivered in novel ways, such as according to circadian rhythms—along with nutrition and supplementation, fitness and mind-spirit instruction. The program is highly individualized and provides care to people with any kind of cancer.

Despite a higher proportion of younger and relapsed patients, survival of metastatic breast cancer patients at the Block Center was approximately double that of comparison populations and possibly even higher.

A collaborative research group looked at survival data for a consecutive case series of 90 women with advanced metastatic breast cancer who received this comprehensive treatment program at the Block Center. Findings:\(^\text{2}\)

Despite a higher proportion of younger and relapsed patients, survival of metastatic breast cancer patients at the center was approximately double that of comparison populations and possibly even higher compared to trials published during this period. Explanations for the advantage relative to conventional treatment alone may include the nutritional, nutraceutical [relating to foods with medicinal properties beyond their nutritional value], exercise and psychosocial interventions, individually or in combination; self-selection of patients cannot be ruled out.
The researchers propose that the doubling of survival in those treated with the integrative program may be physiologically based and not due to self-selection. For example, patients in this program followed a low-fat diet, demonstrated in randomized controlled trials to improve relapse-free survival. Other specific program elements that may have helped with either prolonged survival or treatment tolerance:

- Increased intakes of antioxidants and phytochemicals
- Improved body composition and weight reduction due to increased exercise
- Reduction of stress hormones with mind-spirit interventions
- Higher intakes of vegetables, fiber and omega-3 fatty acids

The Block Center program also evaluates and supports a patient’s quality of life and mental/spiritual responses to cancer and treatment. “Systematic training is provided in relaxation strategies, cognitive-behavioral interventions, and other approaches to enhance coping skills, pain management and sleep hygiene in order to manage the challenges associated with a cancer diagnosis and to mitigate side effects of chemotherapy, while improving treatment tolerance.”

Being able to tolerate treatment better also means that women may be able to complete the treatment, improving their response and benefits.

The Block Program is explained in great detail in his patient-friendly book: Life over Cancer: The Block Center Program for Integrative Cancer Care.

**Block Center Program Supplements**

Supplements used in the 2009 study of advanced metastatic breast cancer patients:

- Used by all patients:
  - Fish oil
  - Multivitamin-mineral supplement designed for cancer patients
  - Mushroom-based immune supplement
  - A phytochemically rich vegetable and fruit drink
- Other supplements frequently used (individualized):
  - Mixed carotenoids
  - Melatonin
  - Calcium D-glucarate
  - Reishi mushrooms
  - Green tea
  - IV vitamin infusions during chemo to prevent treatment-related nutrient deficiency: Vitamins A, C, D, E, K, B-vitamins; calcium, magnesium and trace minerals
Bastyr Integrative Oncology Care: A Naturopathic Oncology Approach

Naturopathic oncology care is complementary rather than alternative to conventional care, with complementary therapies used in conjunction with conventional treatments. Naturopathic oncologists are oriented to deliver integrative oncology care in tandem with their conventional oncology colleagues. For more information, see our discussion of naturopathic medicine and oncology on the BCCT website: Integrative Medical Systems in Practice in the US and Canada.

BCCT advisor Leanna Standish, ND, is a Fellow of the American Board of Naturopathic Oncology (FABNO) and works within the research institute of the prestigious naturopathic school Bastyr University. Dr. Standish has been leading research studies looking at integrative therapies that naturopathic oncologists provide, as well as the costs and outcomes of that care.

In one study published in 2017, the Bastyr Integrative Oncology Research Clinic (BIORC), in collaboration with Fred Hutchinson Cancer Research Center, followed 324 women of all stages of breast cancer who received integrative oncology care from board-certified naturopathic oncologists in the Seattle area. The most common integrative therapies prescribed:

- *Trametes versicolor* (turkey tail mushroom)
- Mind-body therapies
- Acupuncture
- Injectable therapy (mistletoe, vitamin B complex, IV vitamin C, IV artesunate and IV nutrition and hydration)

The costs ranged from $1594 per year for early stage breast cancer up to $6200 per year for stage 4 breast cancer patients. About 20 percent of that cost was out-of-pocket, with the remainder paid for by insurance or written off by the university. As the researchers point out, “regardless of the stage of breast cancer, integrative [naturopathic] oncology care is low-cost relative to conventional oncology costs. Standard cancer treatments may cost as much as $10,000 to $40,000 per month.”¹⁵ The extra cost of adding complementary therapies to conventional care may be outweighed by the benefits to patients: better quality of life, symptom management and in some cases improved response to conventional treatment.

Since opening in 2009, BIORC has enrolled 704 patients in a separate prospective outcomes study treating breast, lung, colon, pancreatic, brain and skin cancers. One-third are patients with stage 4 cancer. During the study, the natural products used have been intravenous (IV) high-dose vitamin C, IV artesunate, oral curcumin, green tea and *Trametes versicolor* (turkey tail mushroom). Dr. Standish shared with us: “Our median overall survival was excellent compared to other published phase III clinical trials.”¹⁶ Their results for breast cancer have not yet been published.
Bastyr Breast Cancer Study Supplements

No one "Bastyr protocol" exists, as researchers continue to investigate and refine approaches. Supplements used in one Bastyr protocol for breast cancer: 9

- IV artesunate
- IV ascorbic acid (vitamin C)
- *Trametes versicolor* (turkey tail mushroom)
- Tetrathiomolybdate for copper chelation
- Curcumin
- Bromelain
- Quercetin
- Low-dose naltrexone

Dr. Kleef: Hyperthermia, Immunology and Integrative Oncology Program

Dr. Ralf Kleef trained in Germany at an integrative-oriented medical school as well as at Sloan Kettering Cancer Research Institute in New York City as a postdoctoral immunology fellow. He has a clinic in Vienna, Austria, which is on the “short list” of preferred European cancer clinics from Ralph Moss, a leading writer on integrative cancer treatments who publishes The Moss Reports.

Dr. Kleef uses what he calls “Lodoco” (low-dose combination therapy), the use of lower doses of chemotherapy and immunotherapy in combination with complementary therapies such as hyperthermia and artemisinin. He uses chemosensitivity and molecular testing to identify which drugs and natural products are more likely to be active against an individual’s cancer.

In addition to using his integrative approach with people with minimal residual disease, he is also getting early promising results in people who were previously heavily treated for cancer and come to him with stage 4 disease.

Dr. Kleef co-authored and published a case study of a woman with stage 4 triple-negative breast cancer with lung metastasis. Kleef treated this 50-year-old woman with low-dose immune checkpoint inhibitors, hyperthermia and interleukin-2. According to Kleef, “She went into complete remission of her pulmonary metastases with transient WHO I-II diarrhea and skin rash. The patient remained alive for 27 months after the start of treatment, with recurrence of metastases as a sternal mass, and up to 3 cm pleural metastases.” Kleef acknowledges that this is only one case, and urges further research using this protocol, which consists only of [European] approved drugs and treatments.17

Several individuals who have been treated at Kleef’s clinic have reported to us their favorable experiences, including patient advocate and breast cancer survivor Lindsay McDonell, although. See her story on the BCCT website: Lindsay McDonell: Diagnostic Testing.
See the Moss Reports for a more thorough description of Dr. Kleef’s program: Moss Reports (purchase required), and Dr. Moss’s blog post: Lower-dose immune drugs as effective as higher doses.

**Integrative Therapies in Breast 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**

The foods you eat, plus how they’re grown and prepared, have a substantial impact on your body terrain.

**Key Points on Healthier Dietary Patterns**

From BCCT summaries Eating Well and Mediterranean Diet, and from *The Ecology of Breast Cancer:*[^18]

- Beginning in childhood, emphasize eating fruits and vegetables, especially leafy greens and those that are deep orange or yellow.
- Limit total fat to 20 to 35 percent of dietary calories. Different types of dietary fat have different health impacts—see a discussion at right.
- Eat more foods containing omega-3s, especially marine sources containing EPA and DHA.
- Eat low-fat dairy products instead of high-fat options.
- Eat less red meat and avoid processed meats.
- Include traditional, whole-soy foods, including tofu, soy milk and fermented miso and tempeh[^19] in your diet, starting in childhood if possible (but not during infancy). Whole forms of soy are best, while infant soy formula, supplements and highly processed soy foods—such as soybean oil, textured vegetable protein or soy protein isolate used in processed foods—are not recommended.
- Limit refined carbohydrates such as white flour, white rice, juices and sugar. Favor complex carbohydrates from whole grains, beans, vegetables and fruits.
- Add seaweed (sea vegetables) to your diet.

Dr. Keith Block recommends eating medicinal mushrooms, such as shiitake, but also writes: "It is difficult to obtain clinically meaningful quantities of mushroom
phytochemicals from even the healthiest diet, which is why I recommend getting them in the form of extracts.”4 See Cooking Mushrooms: 5 Medicinal Mushrooms You Can Cook With from Organizz.com for guidance on edible medicinal mushrooms.

Dietary Fats: Healthier Choices

For most cancers, in general the recommendation is to eat a low-fat diet consisting of healthy fats (olive oil, nut oils, fish oils) and reduce the unhealthy fats (saturated fats found especially in red meat, trans-fats, and high amounts of omega-6 fatty acids). Limit total fat to 20 to 35 percent of dietary calories.

Different types of dietary fat have different health impacts:

- Polyunsaturated fatty acids are necessary, but typical Western diets have too large a ratio of omega-6 compared to omega-3 fatty acids. Some preliminary research suggests that though omega 6 oils have pro-inflammatory effects, they may also have anticancer properties.20
- Eat quality sources of omega 6 fatty acids, such as whole grains and small amounts of cold-pressed (preferably organic) vegetable oils such as sunflower, grapeseed and soybean oil.
- Eat fewer foods that contain high amounts of omega-6s:
  - Heat-extracted vegetable oils (those that are not expeller or cold-pressed)
  - Conventionally-raised meat, poultry and eggs
  - Processed and fast foods (which often use these oils)
- Replace some of the high omega-6 oils with monounsaturated fatty acids such as extra virgin olive oil.
- Eat low-fat dairy products instead of high-fat options to reduce total calories and saturated fats.
- Eat less red meat and avoid processed meats, which are higher in saturated fats.
- Eat more foods containing omega-3s, such as walnuts and wild-caught salmon and sardines.

Treating the Cancer

Several nutrient and food-preparation factors have been connected to reduced growth and spread of breast cancer. No single component has been found to clearly influence breast cancer development or outcomes.10

- **Vegetables and fruits:** Greater consumption of vegetables and fruits has been associated with lower mortality21 although a prospective Japanese study found than an animal-product diet was associated with a decreased risk of breast cancer morbidity among premenopausal Japanese women.22
- **Carotenoids:** Higher baseline blood levels of carotenoids, such as beta-carotene and lycopene, are associated with improved outcomes following diagnosis and treatment.23
- **Antioxidants**: Use of supplements during chemotherapy or radiation is controversial, with some proposing they counteract the anticancer effect of conventional therapy. A reasonable recommendation based on current data would be to avoid high-dose antioxidants, particularly during chemotherapy and radiation therapy, but to consider them long-term at either lower and more physiological doses, or ideally, through a balanced diet rich in vegetables and whole grains.¹⁰

- **Soy**: Large studies of breast cancer survivors confirm that eating soy in whole food sources (not supplements or highly processed foods) is not associated with increased breast cancer proliferation, doesn’t interfere with tamoxifen and appears to increase the effectiveness of anastrozole.²⁴ Genistein, a soy isoflavone, inhibits angiogenesis (formation of blood vessels to supply tumors).²⁵ A large study of combined data on US and Chinese women found that postdiagnosis soy food consumption of 10 mg/day or more showed a tendency toward a reduced risk of breast cancer-specific mortality.²⁶ Soy food consumption has been associated with better breast cancer survival in other studies.²⁷

- **Omega-3 fatty acids from fish oil**: Women who had been diagnosed and treated for early stage breast cancer who had higher intakes of EPA and DHA from food had a dose-dependent reduced risk of all-cause mortality.²⁸

**Reducing Risk**

Eating a healthy diet that is low in fat and high in fruits and vegetables has been linked to a reduced risk of invasive breast cancer²⁹ and a 25 percent reduced risk of recurrence in post-menopausal women.³⁰ Consuming cruciferous vegetables such as broccoli, kale, Brussels sprouts, and cauliflower shows some evidence of reduced risk of breast cancer.³¹

Another large study (Women’s Healthy Eating and Living study, WHEL) included pre- and post-menopausal women and combined low fat intake with higher levels of fruits, vegetables and fiber. It found no difference in breast cancer recurrence or mortality between groups.³² However, a subsequent meta-analysis, including a secondary analysis of the WHEL study, found a potential benefit of a reduced-fat diet on risk of recurrence, even though not on survival.³³

The meta-analysis includes a recommendation to look at overall dietary patterns as well as physical activity in regard to weight:³³

> As weight gain is a common occurrence following breast cancer diagnosis, and survivors are at increased risk for comorbid conditions such as cardiovascular disease and diabetes, achieving a healthy weight through reductions in caloric intake and increases in energy expenditure through a combination of diet, exercise, and behavioral strategies is encouraged.
Another study involving a large cohort of breast cancer survivors found that maintaining a stable weight in the early years postdiagnosis was associated with the lowest overall mortality risk.\textsuperscript{34}

An investigation involving the Women’s Healthy Eating and Living study concluded that a diet with higher vegetable, fruit, and fiber and lower fat intakes than the five-a-day diet may reduce risk of additional breast cancer events, but only in women not experiencing hot flashes.\textsuperscript{35}

The American Cancer Society recommends a dietary composition of 45–65 percent energy from carbohydrate, 10–35 percent of energy from protein, and 20–35 percent of energy from fat. They emphasize reducing the diet’s energy density by limiting portions of energy-dense foods, such as high-fat and sugary items, in addition to increasing intake of low-energy-dense foods, such as vegetables and fruits.\textsuperscript{33}

Nutrient and food-preparation factors connected to breast cancer:

- Micronutrients:
  - **Carotenoids:**
    - Higher baseline blood levels of carotenoids, such as beta-carotene and lycopene, are associated with lower breast cancer risk.\textsuperscript{36}
    - Lycopene is associated with a lower risk of estrogen-receptor-positive (ER+) and progesterone-receptor-positive (PR+) breast cancers in large, population-based studies.\textsuperscript{37}
    - Lycopene is associated with a lower risk of ER−/PR+ or ER−/PR− breast cancer in pooled analysis of prospective cohort studies.\textsuperscript{38}
    - Beta-carotene is associated with decreased risk in postmenopausal women with high alcohol intake.\textsuperscript{39}
  - **DHA and EPA:** These two omega-3 fatty acids, found in fish and fish oils, may be associated with reduced risks of breast cancer\textsuperscript{40} and of reduced risk of additional breast cancer events in patients with early stage breast cancer.\textsuperscript{28}
  - **Milk and dairy products:** High intake of low-fat dairy foods, especially skim/low-fat milk, was associated with reduced risk of breast cancer in premenopausal women. No association between intake of dairy products, calcium and vitamin D and breast cancer risk was seen in postmenopausal women.\textsuperscript{41}
  - **Trans fats:** The link between trans fats and breast cancer risk is modest.\textsuperscript{42} Consumption of trans fats is consistently associated with higher mortality from all causes.\textsuperscript{43}
  - **Omega-6 fatty acids:** In most studies, although not all, higher amounts of omega-6 fatty acids compared to omega-3s are associated with higher risk of breast cancer. In many people, perhaps in part as a result of genetically determined fatty acid metabolism, a higher omega 6:3 ratio is associated with higher levels of inflammation.\textsuperscript{44}
  - **Food preparation:** Charring food (such as on the grill or in a broiler) produces known carcinogens such as heterocyclic amines, which are associated with breast cancer risk.\textsuperscript{45}
  - **Green tea:** Lower breast cancer recurrence is seen with intake greater than three cups per day; less consistent evidence regarding reduced risk of onset.\textsuperscript{46}
• **Soy**: Eating traditional (whole) soy products is associated with lower breast cancer risk, and eating them in childhood is associated with even lower breast cancer risk than soy in adulthood. A large study of combined data on US and Chinese women found that postdiagnosis soy food consumption of 10 mg/day or more showed a significant reduced risk of recurrence. Other studies show lower recurrence of breast cancer with soy consumption, even among postmenopausal women treated with tamoxifen. However, in HER2 positive breast cancer patients, soy consumption has been associated with a greater risk of recurrence, and overexpression of genes that promote cell proliferation.

• **Seaweed and edible mushrooms**: Eating some varieties of seaweed and mushrooms (maitake and reishi) may be associated with lower breast cancer risk.

**Optimizing Your Terrain**

- Proanthocyanidins, found in berries and grapes, are associated with lower inflammation, a contributor to breast cancer risk.

- Refined carbohydrates and insulin sensitivity: Diets with excessive refined carbohydrates cause repetitive spikes in insulin and increase the risk of diabetes, which increases the risk of breast cancer. Elevated insulin levels also promote breast cancer. Improving insulin sensitivity in those with insulin resistance or elevated fasting blood sugar may be helpful not only in reducing breast cancer risk, but also in reducing risk of recurrence and breast cancer-related death in those diagnosed with breast cancer.

See BCCT’s summary Eating Well and chapter 3 of Dr. Ted Schettler's *The Ecology of Breast Cancer: Diet, nutrition, and breast cancer*.18

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**The Ecology of Breast Cancer**

*The Ecology of Breast Cancer: The Promise of Prevention and the Hope for Healing* by BCCT advisor Ted Schettler, MD, MPH, is one of the best sources of information on lifestyle and environment in relation to breast cancer risk and outcomes.

Dr. Schettler proposes that individual body terrain is shaped across the lifespan by all levels, from individual to societal. “Efforts to change the design of that terrain can continue throughout life, so that breast cancer or its recurrence after initial treatment is less likely.”55
Adding Up Benefits

Studies show that while a single lifestyle practice—such as a healthy diet or exercise—show benefit, combining practices is even more powerful.\(^\text{21}\)

Breast cancer patients who adopted a healthier diet and regular exercise lowered their risk of relapse by nearly half, an effect seen in both obese and nonobese women.\(^\text{21}\)

As David Servan-Schreiber explains: “In patients who already have cancer, there is a ‘dose effect’ relationship between regular application of practices that improve lifestyles and the degree of protection from the disease. The more involved these patients are in changing their ‘terrain,’ the greater the benefits.”\(^\text{56}\)

Moving More

From Moving More and *The Ecology of Breast Cancer*:

- The World Cancer Research Fund and the American Institute for Cancer Research both recommend 60 minutes of moderate-intensity or 30 minutes of vigorous-intensity exercise daily to reduce cancer risk. The American College of Sports Medicine recommends that healthy adults and cancer survivors engage in a minimum of 30 minutes of moderate-intensity exercise five days a week for health promotion.
- Even modest amounts of activity provide benefit, so starting slowly with lower intensity exercise and gradually increasing the intensity and duration is a good approach for people who have not been very active.
- Most studies show that the benefits of physical activity are heightened by increasing the activity level and duration.
- Sedentary living increases the risk of many diseases and earlier death. Prolonged sitting is unhealthy, regardless of physical activity levels at other times.

Patients may achieve higher fitness levels in a supervised program compared to a self-directed program.\(^\text{57}\)

See BCCT’s Moving More summary and pages 173-174 of Dr. Ted Schettler’s *The Ecology of Breast Cancer*\(^\text{18}\) for tips for meeting these exercise and movement recommendations.

Treating the Cancer

Moving—whether by formal exercise or by increasing daily activities such as walking, gardening or dancing—is associated with better treatment outcomes. “Most but not all studies show that women who regularly exercise after breast cancer treatment experience reduced all-cause and breast-cancer specific mortality compared to sedentary women over follow-up periods averaging four to eight years. In many
studies, higher levels of physical activity or exercise before diagnosis are also associated with improved survival after diagnosis.58

Breast cancer survivors who performed the equivalent of walking three to five hours per week at an average pace had a lower risk of death from breast cancer as well as death from any cause.59 Conversely, an investigation of the After Breast Cancer Pooling Project found that very low physical activity was associated with a 22 percent increased risk of breast cancer mortality.60 Another analysis from the same project found that engaging in at least 10 MET-hours per week of physical activity was associated with a 27 percent reduction in all-cause mortality and a 25 percent reduction in breast cancer mortality compared with women who were less active.61 Ten MET-hours per week is represented by any one of these activities:62
- 3½ hours of housecleaning
- 3 hours of brisk walking
- 2¼ hours of dancing
- 1 to 1½ hours bicycling 10-16 mph

Managing Side Effects and Promoting Wellness

- Regular exercise is beneficial in reducing fatigue and improving physical function after diagnosis and initial cancer treatment.63
- Women with early stage breast cancer who were more active consistently reported lower levels of depression and increased quality of life five years after the intervention compared to those who were less active.64
- Exercise combined with a healthy diet may increase benefit even more.65
- A study in Canada found that exercise improved patients’ chemotherapy completion rate without causing lymphedema or significant adverse events.66
- A 2019 review concluded that Nordic walking—performed with walking poles similar to ski poles—had a significant and positive impact on a number of breast cancer symptoms including lymphedema, physical fitness, disability and morbid perceptions.67

Reducing Risk

- “Strong evidence shows risk reductions of 20 to 80 percent for postmenopausal breast cancer with increasing physical activity,” according to Dr. Schettler.68 The evidence in premenopausal breast cancer isn’t as strong.
- Women who reported participating in at least seven hours of moderate or vigorous physical activity per week had an 18 percent lower risk of breast cancer in the Nurses Health Study, with over 16 years of follow-up. A further study found that lifetime physical activity was associated with lower risk of premenopausal breast cancer, while both cumulative and recent physical activity were associated with lower risk in postmenopausal women.69
- Research shows an increased risk of various kinds of cancers among inactive individuals compared to very active people. The strongest associations in women are with postmenopausal breast cancer and cervical cancer.70
For a discussion of the many studies examining links between activity and breast cancer, see chapter 4 of Dr. Ted Schettler’s *The Ecology of Breast Cancer: Exercise, physical activity, and breast cancer.*

Managing Stress

As we discuss in BCCT’s Managing Stress summary, unusual or chronic unmanaged stress—and the subsequent alteration in stress biochemistry—can affect tumor growth and proliferation.

Treating the Cancer

In *The Ecology of Breast Cancer,* Dr. Ted Schettler suggests that chronic stress could speed the growth and development of an undiagnosed cancer.

Dr. Schettler points out that the most significant associations of reduced stress levels with better survival are in women who don’t have metastatic disease when they are initially diagnosed and treated. But even in those with more advanced breast cancer, stress reduction has been related to longer survival in some individuals.

Managing Side Effects and Promoting Wellness

Compelling evidence shows that stress reduction significantly improves quality of life after initial treatment of breast cancer and beyond.

Improved quality of life is clearly associated with stress reduction in women with all stages of breast cancer. In general, outcomes are more likely to improve when conventional therapy is combined with more comprehensive interventions that include stress reduction along with optimizing diet, exercise, sleep, and social support.

Therapies for Managing Stress

Several therapies have demonstrated effectiveness in reducing anxiety and stress:
- Sleeping well
- Sharing love and support, shown to substantially help reduce the stress response and improve outcomes in women with breast cancer
- Mind-body approaches
- Manipulative and body-based therapies
- Energy therapies
- Pharmacologic agents such as beta-blockers (see BCCT’s Propranolol summary) and psychedelics (see BCCT’s Inocybeumbrinella (Psilocybin) summary)

See Managing Stress and chapter 7 in Dr. Ted Schettler's *The Ecology of Breast Cancer: Stress, social support, and breast cancer.*
Sleeping Well

Many women diagnosed with and being treated for breast cancer report having sleep difficulties. Anxiety and side effects of treatment can lead to sleep disruption. A vicious circle of cancer symptoms and treatment side effects can build, leading to poor sleep quality. Poor sleep then causes or worsens other symptoms, including depression, fatigue and anxiety.

Treating the Cancer

One of the problems of sleep disruption is that rhythms of the stress hormone cortisol are thrown off target. These abnormal rhythms are linked to less active natural killer cells, which is associated with shorter survival in those with breast cancer.72

Managing Side Effects and Promoting Wellness

Sleep interacts with treatments to impact your quality of life, and it can affect your ability to rebound from rigorous treatments. Repeated chemotherapy treatments impair melatonin production at night, increasingly disrupting sleep cycles as treatment continues.73 Strategies to improve disturbed sleep before starting chemotherapy may improve daily function.74

Many complementary therapies can help improve sleep and subsequently improve symptoms and quality of life. For instance, mind-body practices such as mindfulness meditation, tai chi and stress reduction practices have been found not only to improve sleep, but also to improve fatigue and depression in women with breast cancer.75

Reducing Risk

When circadian rhythms are disrupted by conditions such as shift work, short sleep duration, and exposure to light at night, we see increased risk of several cancers, including breast cancer.76

Optimizing Your Terrain

Beyond affecting normal cortisol rhythms, chronic poor sleep can disrupt many other processes and conditions with the internal terrain, fostering cancer growth and spread.

Consistently poor sleep (and even too much sleep) can lead to a host of physical, mental and emotional problems. Several of these problems create an internal environment that is hospitable to cancer development, growth and spread, such as these:

- Increased inflammation
- Weakened immunity
- Insulin resistance

Tai chi can reduce inflammatory markers in breast cancer survivors with insomnia. Inflammation is a risk factor for cancer.77
Sleeping well is an often overlooked but incredibly important way of keeping yourself healthy and reducing your risk of disease. See BCCT’s Sleeping Well summary.

Creating a Healing Environment

Exposures to toxic chemicals, light at night, radiation and electromagnetic fields are all associated with breast cancer.

Treating the Cancer

Lifetime cigarette smoking is associated with a poor prognosis among women diagnosed with breast cancer, and with breast cancer-specific and all-cause mortality.78

Night shift work is associated with tumor growth: “Women who have breast cancer should be advised not to work night shifts because of the strong experimental evidence showing that suppression of melatonin secretion can facilitate tumor growth.”79

Radiation to treat cancer can increase risk of a second cancer in vulnerable healthy tissue that falls in the treatment field. Some integrative oncology clinicians recommend specific complementary approaches to prevent or minimize ionizing radiation damage to normal cells from imaging or radiation therapy.

- Naturopathic physician Neil McKinney has a protocol using “radio-protectant” natural products.80
- Dr. Keith Block discusses using radiation couplers to minimize damage to normal cells while enhancing killing effects on cancer cell.81

Reducing Risk

Chemical Exposures

Many toxic chemical exposures throughout the lifespan—starting with fetal development—increase the risk of breast cancer. For instance, exposing a fetus to the hormone DES increases breast cancer risk decades later, as does pre-pubertal exposure to the pesticide DDT, including exposures in utero.82

According to a report from the Institute of Medicine, the strongest evidence indicates the following chemical exposures increase breast cancer risk:83

- Combination hormone therapy products (see more below in Reducing Risk)
- Current use of oral contraceptives
- Tobacco smoking

Increasingly persuasive evidence links the following chemical exposures to breast cancer risk:

- Passive smoking
- Organic solvents besides ethanol
- Ethylene oxide
- Polycyclic aromatic hydrocarbons (PAHs)
- 1,3 butadiene
- Some agricultural chemicals
See chapter 5 of Dr. Ted Schettler’s *The Ecology of Breast Cancer: Environmental chemicals, contaminants, and breast cancer.*

BCCT’s *Creating a Healing Environment* summary describes specific actions you can take to improve your environment and reduce harmful exposures. You can also find recommendations on pages 176-180 of *The Ecology of Breast Cancer.*

Night Work and Light at Night
Shift work that disrupts circadian rhythms has been classified as probably carcinogenic by the International Agency for Research on Cancer (IARC). Working night shifts for 20 years or more is associated with a significantly increased risk of breast cancer. The risk with shorter spans of night-shift work is still unclear.

Steps that night shift workers can take to minimize circadian disruption, helping reduce cancer risk:

- Rapidly rotating shifts (one or two consecutive nights) cause less disruption of circadian rhythms than slowly rotating shifts (three or more consecutive shifts).
- Delay of circadian phase (scheduling sleep to start later) causes less disruption than advance of circadian phase (scheduling sleep to start earlier). Therefore, forward- rather than backward-rotating shifts are preferable. For example, scheduling work start times progressing later into the day or night—8pm, then midnight, then 6am—is less disruptive that start times that become earlier: 6am, then midnight, then 8pm.
- Permanent night work is an option to avoid circadian disruption and may be feasible if a night-oriented rhythm during days off is maintained. However, this requires avoiding bright light during the day and making certain that sleep is adequate.
- Modified light intensity during work at night can help, such as working in bright white light to increase adoption of a night rhythm or in dim red light to prevent adoption. Dim red light suppresses melatonin less than bright white light, but with a trade-off in alertness that is critical for performing many tasks.
- People working at night should be especially attentive to maintaining adequate levels of vitamin D.
- Considering the potential risks and benefits, most analysts do not recommend earlier or more intensive mammography screening in women night shift workers.

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**Circadian Rhythms and Breast Cancer**

We describe the dangers of disrupting circadian rhythms (including sleep disruption) and how this can lead to multiple health problems and heighten cancer growth, proliferation and spread in these BCCT summaries:

- Body Terrain and Tumor Microenvironment
- Creating a Healing Environment
- Managing Stress
- Sleeping Well
Ionizing Radiation
Ionizing radiation is clearly established as a risk factor for breast cancer, although very few people, nor even many physicians, are aware of the association.\textsuperscript{86}

Exposure to ionizing radiation from medical sources, including X-rays, CT scans and other medical imaging, is increasing.

Electromagnetic Fields
The International Agency for Research on Cancer (IARC) has classified both extra low frequency (ELF) and radio frequency (RF) electromagnetic fields as possibly carcinogenic in humans,\textsuperscript{84} although the connection to increased risk of breast cancer is not yet clear.

Disturbing case reports of breast cancer in young women carrying cell phones in their bras are noted, but no systematic study of the association has been published. Several mechanisms for how EMFs could influence breast cancer risk have been proposed. Because of this potential risk, many sources propose erring on the side of caution and reducing exposure to ELF-EMFs.

See BCCT’s Creating a Healing Environment summary and chapter 6 of Dr. Ted Schettler’s \textit{The Ecology of Breast Cancer: The electromagnetic spectrum and breast cancer: Sunlight and vitamin D; shift work, artificial light, and sleep; electromagnetic fields}\textsuperscript{18} for tips for reducing exposures.

Sharing Love and Support

Treating the Cancer
Sharing love and support has been shown to substantially help reduce the stress response and improve outcomes in women with breast cancer.\textsuperscript{87}

A 2017 investigation of the After Breast Cancer Pooling Project found that larger social networks were associated with better breast cancer-specific and overall survival.\textsuperscript{88}

Managing Side Effects and Promoting Wellness
Some of the earliest and most pivotal studies of social support improving quality of life have been in women with breast cancer.\textsuperscript{89}

See BCCT’s Sharing Love and Support summary.

Exploring What Matters Now

Treating the Cancer
Finding meaning and setting goals are associated with better outcomes. Results of some studies:
• A study of 578 women with early-stage breast cancer were assessed using the mental adjustment to cancer (MAC) scale. The researchers found a “significantly increased risk of relapse or death at five years in women with high scores on the helplessness and hopelessness category of the MAC scale compared with those with a low score in this category.”

• A small study of metastatic cancer of many types found extended survival among those who scored higher on these scales:
  o Ability to act and change
  o Willingness to initiate change
  o Participating in self-help work
  o Relationships with others
  o Quality of experience

• Another study of patients with many types of cancer concluded that longer-term survivors displayed a much higher degree of early involvement in their psychological self-help than did most of their nonsurviving peers.

Managing Side Effects and Promoting Wellness

Finding meaning, setting goals, allowing and accepting difficult emotions and connecting with spirituality are associated with better outcomes:

• Suppressing difficult emotions is associated with greater distress in those with breast cancer.
• A 2015 study found that a "meaning/peace factor of spirituality" was consistently associated with improved quality of life (overall, physical and mental).

See BCCT’s Exploring What Matters Now summary.

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 breast cancer.

Several therapeutic approaches show potential. However, because breast cancer is actually many individual diseases with different responses to treatments, the advice of a healthcare professional knowledgeable about integrative oncology therapies is crucial.

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 breast cancer, where to find dosing guidelines, cautions, and their use in integrative protocols, programs and systems. A licensed health professional experienced in integrative breast 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.

We limit our presentation here to therapies with clinical evidence—studies involving cancer patients—and not solely cell or animal evidence (see below). Preclinical evidence is included in therapy summaries on this site for those who wish to assess that.

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**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 breast 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

The role of each of the 7 Healing Practices in arresting or reducing breast cancer growth and spread is described above.

Conventional Breast Cancer Therapies

Conventional treatment for breast cancer is becoming more and more specific, depending on the type, stage and characteristics of a person’s cancer. For a growing number of women, treatment is effective or even curative, especially in the case of early-stage cancer.

The National Comprehensive Cancer Network (NCCN) professional guidelines for breast cancer treatment provide enough treatment guideline scenarios to make your head spin. Fortunately, NCCN has provided patient-friendly guides in which you can look up your type and stage of breast cancer and see treatment options your doctors are likely to present to you. See "Further Clinical Practice Guidelines" above.

A few key points from these guidelines:
- Getting the diagnosis and the tumor characteristics right is absolutely key to figuring out the best conventional treatment approach. See Standard and Non-standard Diagnostic Approaches on the BCCT website.
- According to breast cancer medical advocate and BCCT Advisor, Gwen Stritter, MD, the NCCN guidelines are really good for about 85 percent of primary [non-metastatic] breast cancers. Following the guidelines will result in response to treatment for those 85 percent of patients. Since early-stage primary cancer is likely curable by following the guidelines, the risk/benefit analysis does not favor straying from them.
- A conventional oncology doctor is not likely to stray from the NCCN guidelines.
- Although advanced breast cancer is incurable in most cases, steady improvements are seen in survival with standard therapies as well as the newer targeted agents. We at BCCT know of many women who have lived for years
with recurrent or advanced breast cancer behaving like a chronic illness kept at bay at least in part by conventional treatment.

This is not to say that conventional treatments are magic bullets that get in there, destroy the cancer cells, and get out without being noticed. All these treatments—surgery, chemotherapy, radiation therapy, hormone therapy and immunotherapy—come with costs: physical, cognitive, emotional, social, spiritual and financial. And they don’t work for everyone all the time.

Similarly, no complementary or alternative therapy is a suitable stand-alone treatment for breast cancer. Integrating the best of both evidence-based conventional and complementary therapy may be a sensible way to bolster the effects of conventional treatment and improve your tolerance to the side effects so you can complete your treatments. This integrative approach also makes sense for reducing the risk of recurrence after treatment and possibly extending your life, as described in sections below.

Ralph Moss’ free The Ultimate Guide to Cancer:™ Do-It-Yourself (DIY) Research shows you how to use four of the main tools that doctors use to decide on the best cancer treatments. It will help you learn why some cancer treatments that look good in clinical trials may not work for “real world” patients like yourself. It will help you answer two questions that the doctor may be hesitant to answer in the detail you need to decide about treatment:

- What are my chances of actually living longer if I use this treatment?
- What are the likely side effects, and how long will they last?

A starting place for the science and conventional therapies related to breast cancer:

- National Cancer Institute:
- Breastcancer.org, https://www.breastcancer.org/

Natural Products

BCCT advisor Debu Tripathy, MD, writes that “herbal and botanical agents have significant potential as bioactive agents that can affect cellular pathways involved in breast cancer, but may also cause side effects and drug interactions. . . Caution should be exercised when used with other treatments.”

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

These therapies may be widely used in integrative cancer protocols and traditional medical systems.
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| Flaxseed lignans          | • Anticancer effects among newly diagnosed breast cancer patients, including reduced tumor growth\(^95\)  
                            • Lower mortality among breast cancer patients in observational evidence\(^96\) |
| Melatonin                 | • Increased survival time in breast and several other types of cancer\(^97\)  
                            • Did not increase the toxicity of tamoxifen, and enhanced the efficacy of chemotherapy and reduced its toxicity\(^97\)  
                            • Several anticancer mechanisms in preclinical studies\(^97\)  
                            • Caution on use shortly before surgery as it can magnify the effects of anesthesia\(^4\) |
| Turkey tail mushroom      | • Extended survival in patients with certain types of breast cancer\(^98\)  
                            • Improved survival curve of people with operable breast cancer with vascular invasion\(^99\)  
                            • Increased natural killer (NK) cells and other cancer-killing cells in breast cancer patients\(^100\)  
                            • Enhanced effectiveness of chemotherapy and radiation therapy against cancer cells while protecting normal cells\(^100\) anticancer effects resulting in reduced tumor growth and metastasis in animals\(^100\) |
| Vitamin D (in doses up to 4000 IU per day for adults) | • Deficiency is associated with these outcomes:  
                            ○ Lower odds of successful breast cancer treatment\(^101\)  
                            ○ Breast cancer metastasis\(^102\)  
                            • Higher vitamin D status is strongly associated with better breast cancer survival\(^103\)  
                            • Vitamin D supplementation plays an important role in disease-free survival in a number of cancers, particularly breast\(^104\) |

Group 2: Good clinical evidence of efficacy & safety, limited access  
Some may require a prescription, for example.

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| Mistletoe | • Improved tumor response and reduction with chemotherapy, enhanced survival rates and prolonged relapse intervals\(^105\)  
            • Requires a prescription from a licensed physician  
            • May not be easily available in the US |
Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

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| Ginseng               | • Improved survival in breast cancer patients in epidemiological data\(^{106}\)  
                       | • Used in the MacDonald breast cancer program\(^{8}\)                                                                                                                                                         |
| Maitake mushroom      | • Increased cancer regression in patients with advanced breast cancer\(^{52}\)  
                       | • Antitumor activity preventing cancer development and metastasis\(^{52}\)  
                       | • Used in these programs and protocols:  
                        | o Alschuler & Gazella complementary approaches\(^{3}\)                                                                                               |
                       | o Block program\(^{4}\)  
                       | o MacDonald breast cancer program\(^{8}\)                                                                                                           |
                       | • Used in traditional Chinese medicine                                                                                                                                                                      |
| Omega-3 fatty acid supplements | • Conflicting interactions with chemotherapy reported:  
                       | o Improved outcomes with DHA added to chemotherapy in a small trial of metastatic breast cancer patients\(^{40}\)  
                       | o Increased resistance to chemotherapy; not recommended on the days surrounding chemotherapy\(^{107}\)  
                       | • No adverse side effects and possible improved anthracycline-based chemotherapy outcome\(^{108}\)  
                       | • Promoted cell death (apoptosis) and reduced proliferation in preclinical studies\(^{109}\)  
                       | • Used in the MacDonald breast cancer program\(^{8}\)                                                                                               |
| Vitamin C             | • Decreased overall mortality and breast cancer mortality from use post-diagnosis\(^{110}\)  
                       | • Inhibited proliferation of human breast cancer cells in conjunction with retinoic acid\(^{111}\)  
                       | • Decreased cell viability of all breast cancer cell lines with intravenous (IV) vitamin C, with greater results when used with eribulin mesylate, tamoxifen or fulvestrant\(^{112}\)  
                       | • May interact with conventional treatments (see antioxidant supplements in Group 4 below);\(^{113}\) however, intravenous vitamin C does not appear to increase toxicity or interfere with antitumor effects of gemcitabine/erlotinib therapy or paclitaxel and carboplatin\(^{114}\)  
                       | • Used in the Block program\(^{4}\) to enhance chemotherapy effectiveness                                                                                                                                    |
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.

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<tr>
<th>Therapy</th>
<th>Notes</th>
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</thead>
</table>
| **Antioxidant supplements** (including beta-carotene, lutein, lycopene, selenium, vitamin A, oral vitamin C, vitamin E and others) | • Improved survival with post-treatment use of any antioxidant supplements among breast cancer survivors\(^{115}\)
• Use during chemotherapy or radiation is controversial, with some proposing they counteract the anticancer effect of conventional therapy.\(^{116}\) A reasonable recommendation based on current data is to avoid high-dose antioxidants, particularly during chemotherapy and radiation therapy, but to consider them long-term at either lower and more physiological doses, or ideally, through a balanced diet rich in vegetables and whole grains.
• Increased mortality in mixed studies of healthy individuals and those with various diseases taking beta-carotene or vitamin E supplements, and possibly vitamin A supplements\(^ {117}\) |
| **Coenzyme Q10** | • Case reports of regression of breast cancer metastases\(^ {118}\)
• May reduce effectiveness of radiation therapy\(^ {119}\)—BCCT's naturopathic physician sources advise not to take during radiation therapy\(^ {120}\)
• Other cautions are noted with long-term use of high doses\(^ {5}\)
• Used in these programs and protocols:
  o Alschuler & Gazella complementary approaches\(^ {3}\)
  o Block program\(^ {4}\)
  o MacDonald breast cancer program\(^ {8}\)
  o McKinney protocols\(^ {9}\) |
| **DIM (diindolylmethane)** | • Beneficially modulated levels of sex hormone binding globulin and endogenous estrogens in breast cancer patients on tamoxifen, but the impact on cancer survival is unknown\(^ {121}\)
• Antiproliferative effects in lab and animal studies\(^ {122}\) |
| **Iodine** | • Improved five-year disease-free survival in a pilot study\textsuperscript{125}  
• Decreased the invasive potential of a triple negative basal cancer cell line and activated the antitumor immune response, preventing progression in preclinical studies\textsuperscript{126} |
| **Reishi mushroom** | • Enhanced treatment response with chemo- and radiotherapy in cancer patients\textsuperscript{127}  
• Toxic effects in powder form to the liver\textsuperscript{128}  
• Notable preclinical evidence:  
  o Suppressed breast cancer cell invasion, growth, migration and metastasis in cell and animal studies\textsuperscript{129}  
  o Mixed and inconsistent toxic effects on human leukocytes\textsuperscript{130}  
• Used in these programs and protocols:  
  o Alschuler & Gazella complementary approaches\textsuperscript{3}  
  o Block program\textsuperscript{4}  
  o MacDonald breast cancer program\textsuperscript{8}  
• Used in traditional Chinese medicine |
| **Vitamin E** | • Inconsistent impacts on mortality reported:  
  o Doses greater than 400 IU/day increased all-cause mortality, mostly in patients with chronic diseases\textsuperscript{131}  
  o No increase in mortality at doses up to 800 IU/day in apparently healthy people\textsuperscript{132}  
  o Increased mortality in mixed studies of healthy individuals and those with diseases\textsuperscript{117}  
• Some concerns about interfering with chemotherapy and radiation therapy (see antioxidant supplements above)  
• Specific forms of vitamin E such as \( \gamma \)-tocopherol (\( \gamma \T \)), \( \delta \)-tocopherol (\( \delta \T \)), \( \gamma \)-tocotrienol (\( \gamma \TE \)) and \( \delta \)-tocotrienol (\( \delta \TE \)) can inhibit the growth and induce death of many types of cancer cells and |
are capable of suppressing cancer development in preclinical cancer models\textsuperscript{133}
- Used in these programs and protocols:
  - Alschuler & Gazella complementary approaches\textsuperscript{3}
  - MacDonald breast cancer program\textsuperscript{8}

**Vitamin K**
- Reduced adhesion and proliferation of breast cancer cells with vitamin K\textsubscript{2}\textsuperscript{134}
- Conflicting results regarding mortality from dietary sources of vitamin K:
  - Reduced risk of cardiovascular, cancer, or all-cause mortality\textsuperscript{135}
  - Not associated with all-cause mortality, cancer mortality or mortality from other causes\textsuperscript{136}

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

<table>
<thead>
<tr>
<th><strong>Therapy</strong></th>
<th><strong>Notes</strong></th>
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</thead>
<tbody>
<tr>
<td>Fermented wheat germ extract</td>
<td>- Anticancer and anti-metastatic effects in animal trials and a few clinical trials, but not breast cancer\textsuperscript{137}</td>
</tr>
<tr>
<td></td>
<td>- Enhanced the efficacy of tamoxifen in inducing cell death (apoptosis) in ER\textsuperscript{+} breast cancer cells\textsuperscript{138}</td>
</tr>
<tr>
<td></td>
<td>- Enhanced estrogen-receptor (ER) activity alone, with further decreased ER activity beyond tamoxifen’s effect in cells when used with tamoxifen\textsuperscript{139}</td>
</tr>
<tr>
<td></td>
<td>- In Ralph Moss’s Top 10 list of supplements</td>
</tr>
<tr>
<td></td>
<td>- Used in Alschuler &amp; Gazella complementary approaches\textsuperscript{3}</td>
</tr>
<tr>
<td>Indole-3-carbinol (I3C)</td>
<td>- Reactivated PTEN, a potent tumor suppressor gene, in mice, leading to potent suppression of tumor development\textsuperscript{140}</td>
</tr>
<tr>
<td></td>
<td>- Sensitized multidrug resistant tumor cells to doxorubicin and vinblastine in cell\textsuperscript{141} and animal studies\textsuperscript{142}</td>
</tr>
<tr>
<td></td>
<td>- Reduced proliferation, induced cell death (apoptosis) and other anticancer effects in lab evidence\textsuperscript{143}</td>
</tr>
<tr>
<td></td>
<td>- Synergistic effect with tamoxifen\textsuperscript{144} or fenretinide\textsuperscript{145} inhibiting the growth of an estrogen-dependent human breast cancer cell line</td>
</tr>
<tr>
<td></td>
<td>- Promoted cell death (apoptosis) in metabolically stressed cancer cells; the effect was enhanced when used with genistein\textsuperscript{146}</td>
</tr>
<tr>
<td></td>
<td>- Reversed cytotoxicity of dexamethasone (I3C acid condensation derivatives) in lab tests\textsuperscript{147}</td>
</tr>
</tbody>
</table>
| Isothiocyanates | • Inhibited tumor cell growth, promoted cell death (apoptosis) and inhibited angiogenesis (formation of blood vessels to feed tumors) in lab and animal studies\(^\text{148}\)  
• Reduced cell survival and and inhibited cell migration, reducing the metastatic potential of breast cancer cells, when combined with lapatinib, even with drug-resistant cells\(^\text{149}\) |
| Medical cannabis and cannabinoids | • Reduced breast tumor growth and promoted tumor cell death (apoptosis) in cell and animal studies, as well as reduced metastasis and angiogenesis (blood vessel growth to supply tumors) in animal studies\(^\text{150}\) (although some individual cannabinoids promote breast cancer growth) |
| L-theanine | • Enhanced effects of some chemotherapy drugs in animal studies\(^\text{151}\) |
| Modified citrus pectin | • Inhibited the formation of metastatic deposits in lungs and bones of human breast and prostate carcinoma cells in animals\(^\text{152}\) |
| Shiitake mushroom | • Inhibited human breast tumor growth in cell studies\(^\text{153}\) and in mice\(^\text{154}\) |

Other therapies with preclinical evidence only for treating the cancer

- Amooranin
- Artemisinin
- Ashwagandha
- Astragalus
- Bromelain
- Cannabidiol
- Calcium D-glucarate
- Clarithromycin
- Curcumin
- Gossypol
- Grape seed extract
- Green tea extract / EGCG
- Inositol hexaphosphate
- Metformin and heme
- Milk thistle
- Noscapine
- Pomegranate
- Quercetin
- Resveratrol
- Scutellaria barbatae
- Triphala (mixture of amla, bibhitaki and hariaki)
Group 6: Evidence of no efficacy or may be dangerous

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
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<tbody>
<tr>
<td>714-X</td>
<td>• Not substantiated in animal studies or based on any available human evidence[^155]</td>
</tr>
<tr>
<td>Amygdalin (Laetrile®)</td>
<td>• Little anticancer activity in animal studies and no anticancer activity in human clinical trials[^156]</td>
</tr>
<tr>
<td></td>
<td>• Considerable risk of serious adverse effects from cyanide poisoning[^157]</td>
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<td></td>
<td>• Banned in the United States, the UK and Europe but available in other countries and online[^158]</td>
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<tr>
<td>Essiac tea or Flor-Essence</td>
<td>• Promoted mammary tumor development in rats[^159]</td>
</tr>
<tr>
<td></td>
<td>• Stimulated cancer cell proliferation in both estrogen receptor positive and estrogen receptor negative cell lines[^160]</td>
</tr>
<tr>
<td></td>
<td>• Inconclusive preclinical, animal, and laboratory results regarding anticancer effects[^161]</td>
</tr>
<tr>
<td>Glutathione</td>
<td>• May increase resistance to cancer chemotherapy drugs such as cisplatin[^162] similar effects are found with glutathione precursor n-acetyl L-cysteine[^163]</td>
</tr>
<tr>
<td></td>
<td>• May interfere with active cancer therapies which depend on a pro-oxidant and glutathione-depleting effects:</td>
</tr>
<tr>
<td></td>
<td>o Depletion of glutathione shows improved response to radiation[^164]</td>
</tr>
<tr>
<td></td>
<td>o Inhibiting glutathione synthesis may prevent chemoresistance in triple-negative breast cancer[^165]</td>
</tr>
<tr>
<td>High-dose oral vitamin C</td>
<td>• Ascorbic acid can reach only a limited plasma concentration through oral administration; high doses administered intravenously show better effect</td>
</tr>
<tr>
<td>Hydrazine sulfate</td>
<td>• Ineffective in clinical trials[^166]</td>
</tr>
<tr>
<td></td>
<td>• Many hydrazines are known to cause cancer, including mammary cancer in animals[^167]</td>
</tr>
<tr>
<td>L-glutamine</td>
<td>• Serves a role in promoting tumor cell growth and maintenance such that cancer cells are said to exhibit “glutamine addiction”[^168]</td>
</tr>
<tr>
<td>Shark cartilage or Neovastat</td>
<td>• No responses in studies of advanced cancers, including breast cancer[^169]</td>
</tr>
</tbody>
</table>
Soy supplements and isoflavone isolates
See discussions of beneficial whole soy foods above in Eating Well

- Increased expression of genes associated with increased cell proliferation and cell cycle progression in women with invasive breast adenocarcinoma\textsuperscript{50}
- Associated with breast cancer risk or progression\textsuperscript{170}
- Induced estrogen-dependent tumor cell growth and increased breast cancer-associated aromatase expression and activity in preclinical studies\textsuperscript{171}
- Promoted breast cancer metastasis in preclinical studies\textsuperscript{172} (Note that the authors of this study state the use of "dietary soy isoflavones", but the use described is similar to taking soy supplements and is not representative of eating whole soy foods.)

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

Off-label drug use involves a physician prescribing a drug for a disease or condition not approved by the FDA. Prescribing drugs off-label is legal if sufficient evidence indicates its usefulness for the condition or disease prescribed. However, different state medical boards have varying standards regarding off-label use of specific drugs.

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

Some may require a prescription, for example.

<table>
<thead>
<tr>
<th>Therapy</th>
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| Bisphosphonates, including clodronate and zoledronic acid | - Reviews published in 2017 found these effects:\textsuperscript{173}  
  o Reduced risk of bone metastases and increased survival in women with early breast cancer  
  o Increased survival, including disease-free survival, in postmenopausal women with nonmetastatic breast cancer, but not premenopausal women  
  o No evidence of effect on bone metastases or overall survival in women with advanced breast cancer without clinically evident bone metastases  
  - Reduced incidence and number of new metastases in women with breast cancer at high risk for distant metastases\textsuperscript{174}  
  - Recommended in a Cancer Care Ontario and American Society of Clinical Oncology clinical practice guideline\textsuperscript{175}  
  - Findings with zoledronic acid:  
    o Reduced defective immune function in newly diagnosed breast cancer patients\textsuperscript{176} |
| Propranolol and other beta blockers | Reduced breast cancer progression and mortality in a large population study in Ireland\textsuperscript{180}  
Reduced breast cancer deaths although not all-cause mortality in one meta-analysis\textsuperscript{181} but no survival advantage in other large pooled analyses\textsuperscript{182}  
Decreased risk of breast cancer-related metastasis, and breast cancer death among postmenopausal women with early primary triple-negative breast cancer\textsuperscript{183}  
Reduced the rate of metastasis in breast and other cancers; a 2016 review suggests that propranolol be added to standard of care for nonmetastatic cancers as a strategy to reduce the rate of metastasis. \textsuperscript{184}  
May reduce the effects of stress on primary tumor growth\textsuperscript{184} and establishment of brain metastases\textsuperscript{185}  
Prolonged survival of cancer patients, especially patients with early-stage cancer treated primarily with surgery (not specific to breast cancer)\textsuperscript{186}  
Increased the effectiveness of 5-FU and paclitaxel in preclinical studies\textsuperscript{187}  
Reduced activity of hexokinase-2, an enzyme important for tumor metabolism, in preclinical studies\textsuperscript{188}  
Inhibited invasion of tumor cells and decreased expression of pro-metastatic genes in cell studies (salbutamol)\textsuperscript{189}  
Decreased proliferation, migration, invasion and metastasis in preclinical studies when used with metformin\textsuperscript{190}  
Requires a prescription from a licensed physician |

- When added to letrozole had the highest response rate of 15 treatments for neoadjuvant endocrine therapy for HR positive breast cancer\textsuperscript{177}  
- Enhanced gamma-delta T cells in targeting and killing estrogen-receptor-positive breast cancer cells in preclinical studies\textsuperscript{178}  
- Require a prescription from a licensed physician  
- Clodronate is currently not approved for use in the US, but is approved in 67 other countries.\textsuperscript{179}
Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

<table>
<thead>
<tr>
<th>Therapy</th>
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</table>
| Chronomodulated therapies       | • Reduced toxicity and improved responses to chemotherapy; optimal timing is influenced by the drug and type of cancer\(^1\)\(^{91}\)  
                                 | • Reduced toxicity and improved response to chemotherapy depending on time of day in colorectal patients receiving 5-fluorouracil (FU)\(^1\)\(^{92}\) and in mice received cyclophosphamide and doxorubicin\(^1\)\(^{93}\)  
                                 | • Enhanced antitumor and antimetastatic treatment effects if administered to mice when aldehyde dehydrogenase (ALDH) activity was increased in highly invasive tumors\(^1\)\(^{94}\)  
                                 | • Used in the Block program\(^4\)                                                                                                                                                                      |
| Low-dose naltrexone             | • Tumor shrinkage and extended survival in case studies and preliminary clinical studies with cancers other than breast cancer (see BCCT's Low-dose Naltrexone page)  
                                 | • Requires a prescription from a licensed physician and access from a compounding pharmacy  
                                 | • Used in these programs and protocols:  
                                 |   • Block program\(^4\)  
                                 |   • Elsegood LDN guidelines\(^1\)\(^{95}\)  
                                 |   • McKinney breast cancer protocol\(^9\)                                                                                                                                                         |
| Metformin                       | • Decreased metastatic cases when used with adjuvant therapy in nondiabetic women in a small study\(^1\)\(^{96}\)  
                                 | • Better clinico-pathological properties and nonsignificantly improved disease-free survival in breast cancer patients using metformin at the time of diagnosis\(^1\)\(^{97}\)  
                                 | • Increased survival of breast cancer patients in one meta-analysis\(^1\)\(^{98}\) but not another\(^1\)\(^{99}\)  
                                 | • Increased pathologic complete response rates (the absence of residual tumor at the time of surgery) in diabetic patients with breast cancer receiving neoadjuvant chemotherapy\(^2\)\(^{00}\)  
                                 | • Notable preclinical evidence:  
                                 |   • Resensitized breast cancer cell lines to doxorubicin, either alone or in combination with tamoxifen, and reversed multi-drug resistance\(^2\)\(^{01}\)  
                                 |   • Reduced survival and proliferation of cancer cells, increased radiosensitivity and enhanced tumor response to irradiation\(^2\)\(^{02}\)  
                                 |   • Decreased metastatic cases in preclinical studies\(^2\)\(^{03}\)                                                                                                                                 |
Decreased proliferation, migration, invasion and metastasis in preclinical studies when used with propranolol\textsuperscript{190}

- Requires a prescription from a licensed physician
- Used in these programs and protocols:
  - Block program\textsuperscript{4}
  - Chang strategies\textsuperscript{5}
  - McKinney breast cancer protocol\textsuperscript{9}

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.

<table>
<thead>
<tr>
<th>Therapy</th>
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</table>
| Artesunate                                   | - Long-term use (up to 37 months) in metastatic breast cancer patients did not result in any major safety concerns\textsuperscript{204}  
- Notable preclinical evidence:  
  - Activated cell death (apoptosis) in breast cancer cells\textsuperscript{205}  
  - Highly metastatic breast tumors tend to become resistant to artesunate in cell studies\textsuperscript{206}  
- May cause toxicity, especially liver toxicity, when used with chemotherapy or radiation therapy\textsuperscript{207}  
- Semi-synthetic forms of artemisinin including artesunate are available as FDA-approved drugs for use in patients with a documented case of severe malaria  
- Requires a prescription from a licensed physician |
| Copper chelation with tetrathiomolybdate (TM) | - Improved event-free survival and progression-free survival and decreased cancer biomarkers\textsuperscript{208}  
- May promote breast cancer stem cells, potentially leading to recurrence\textsuperscript{165}  
- Requires a prescription from a licensed physician and access from a compounding pharmacy |
| Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and COXII inhibitors | - Improved disease-free survival in the first few years after surgery with perioperative use of ketorolac\textsuperscript{209}  
- Increased survival with use in some studies\textsuperscript{210} but not in others;\textsuperscript{211} a meta-analysis found a |
nonsignificant trend toward lower risk of mortality with low-dose use of aspirin\textsuperscript{212}

- Reduced size of the primary tumor, improved lymph node status, and fewer involved axillary nodes\textsuperscript{213}
- The US Food and Drug Administration warns that ibuprofen, naproxen and ketorolac increase the risk of having a heart attack or stroke; medical supervision is strongly advised with all NSAIDs.\textsuperscript{214}
- May require a prescription from a licensed physician
- Used in these programs and protocols:
  - Block program\textsuperscript{4}
  - Chang strategies\textsuperscript{5}

<table>
<thead>
<tr>
<th>Statins</th>
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<tbody>
<tr>
<td>Improved recurrence-free, cancer-specific and/or overall survival, particularly with lipophilic statins in one analysis\textsuperscript{215}</td>
</tr>
<tr>
<td>Reduced proliferation and increased cell death (apoptosis) in patients diagnosed with DCIS or stage 1 breast cancer with high grade (poorly differentiated) tumors with fluvastatin use\textsuperscript{216}</td>
</tr>
<tr>
<td>May induce resistance to chemotherapy\textsuperscript{217}</td>
</tr>
<tr>
<td>Associated with serious side effects including permanent muscle damage and impaired cognitive function; their potential benefits in breast cancer must be weighed against the risk, and they should be discontinued promptly if serious side effects occur (see our Statins summary)</td>
</tr>
<tr>
<td>Notable preclinical evidence:</td>
</tr>
<tr>
<td>- Inhibited cancer growth and development in preclinical studies\textsuperscript{218}</td>
</tr>
<tr>
<td>- Requires a prescription from a licensed physician</td>
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</tbody>
</table>

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

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<tr>
<th>Therapy</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Chloroquine (A4M Integrative Cancer Therapies presentation)</td>
<td>Inhibited growth of breast cancer in cell studies and prolonged survival in mouse studies\textsuperscript{219}</td>
</tr>
<tr>
<td></td>
<td>Reduced tumor growth in carboplatin-resistant triple negative breast cancer orthotopic xenografts and targeted cancer stem cells\textsuperscript{220}</td>
</tr>
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<td>Sensitized breast cancer cells to treatment with LY294002 and rapamycin in animal models\textsuperscript{221}</td>
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</table>
Potentiated the anticancer effect of the chemotherapy drug 5-fluorouracil in mice\(^{222}\)

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<thead>
<tr>
<th>Combination therapies</th>
<th>Metformin and propranolol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>o Decreased proliferation, migration, invasion and metastasis in preclinical studies(^{190})</td>
</tr>
</tbody>
</table>

### Diets and Metabolic Therapies

- **Intermittent fasting:** Periodic fasting around the time of chemotherapy may sensitize cancer cells to chemotherapy while protecting normal cells.\(^{223}\)
- **Ketogenic diet:**
  - Clinical evidence is limited to case studies showing improvement or complete responses to ketogenic diets in combination with other therapies.\(^{224}\)
  - In preclinical studies, a low-carbohydrate ketogenic diet slowed mammary tumor growth and increased tumor latency in mice\(^{225}\) and this effect was increased when mice were also treated with metformin.\(^{226}\)
  - Lab studies have found that human breast cancer cells with an enzyme capable of re-using ketone bodies used nearby ketogenic fibroblast cells to fuel their growth.\(^{227}\)

### Therapies Using Heat, Cold, Sound, Light or Cutting-edge Radiotherapy

- **Hyperthermia:**
  - Hyperthermia acts as a chemo- and radio-sensitizer and improves outcomes such as local control and overall survival.\(^{228}\)
  - A 2001 review concluded that “randomized phase III studies performed in patients with breast cancer, malignant melanoma and cervical cancer have convincingly confirmed the increased efficacy of the combination of radiotherapy with local or regional hyperthermia in comparison with radiotherapy alone.”\(^{229}\)

### 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

The role of each of the 7 Healing Practices in managing symptoms, improving quality of life and promoting wellness is described above. Also see the patient brochure Wellness during Tamoxifen Treatment on the BCCT Breast cancer summary.

---

\(^{190}\) \(^{222}\) \(^{223}\) \(^{224}\) \(^{225}\) \(^{226}\) \(^{227}\) \(^{228}\) \(^{229}\)
Conventional Therapies

Vaginal moisturizers and vaginal rings supplying low-dose estrogen are used to address sexual discomfort and difficulties. Although these are conventional therapies, they may not be included in many conventional treatment programs unless or until a patient expresses a need.

Other conventional therapies for managing side effects are widely available. Ask your oncologist or primary care physician for recommendations.

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.

<table>
<thead>
<tr>
<th>Therapy</th>
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<tbody>
<tr>
<td>Bromelain</td>
<td>• Reduced severe joint pain and severe mucosal dryness (in combination with sodium selenite, papain and Lens culinaris lectin) in patients undergoing adjuvant hormone therapy(^{230})</td>
</tr>
</tbody>
</table>
| Coenzyme Q10 | • Improved markers of heart function in patients receiving doxorubicin without reducing doxorubicin’s effectiveness\(^{231}\) (see Taking Care of Your Heart below)  
• Insufficient evidence for relieving fatigue or improving quality of life\(^{232}\) (but see effects when combined with l-glutamine in Group 4 below) |
| Ginger    | • Reduced nausea and vomiting during chemotherapy in most but not all reviews\(^{233}\)—as effectively as metoclopramide but not ondansetron in one study\(^{234}\)—and improved response to antiemetic drugs\(^{235}\) |
| Guarana   | • Improved cancer-related fatigue\(^{236}\)                                                                                               |
| Vitamin D | • Improved bone health when used with calcium in breast cancer patients\(^{237}\) and any women using aromatase inhibitors\(^{238}\)  
• Reduced incidence and severity of joint pain resulting from breast cancer treatment with letrozole\(^{239}\) and other aromatase inhibitors,\(^{240}\) and also reduced disability from aromatase inhibitor-induced arthralgias;\(^{241}\) se of high dose vitamin D\(_2\) maintained bone mineral density as well as reduced pain.\(^{242}\)  
• Increased doses are needed with concomitant steroid uptake.\(^{243}\) |
Group 2: Good clinical evidence of efficacy & safety, limited access

Some may require a prescription, for example.

<table>
<thead>
<tr>
<th>Therapy</th>
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</tr>
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</table>
| Medical cannabis and cannabinoids | • A 2018 review from the National Academy of Sciences, Engineering and Medicine drew these conclusions:244  
  o Effective for treating pain in adults and chemotherapy-induced nausea and vomiting (Conclusive or substantial evidence)  
  o Improved secondary sleep disturbances (moderate evidence)  
  o 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 |
| Mistletoe extract                | • Improved quality of life and functioning245  
  • Reduced chemotherapy side effects such as fatigue, nausea and vomiting, insomnia, appetite loss, breathing difficulty, constipation, diarrhea, oral inflammation and pain246  
  • Improved psychosomatic self-regulation as a measure of autonomous coping with the disease.247  
  • Requires a prescription from a licensed physician  
  • Access in the US is difficult but not impossible |

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Agaricales mushrooms             | • Reduced chemotherapy-induced fever, nausea and vomiting, loss of appetite and changes in bowel function in patients with breast cancer248  
  • Improved quality of life249  
  • Used in these programs and protocols:  
    o Alschuler & Gazella complementary approaches3  
    o Block program4  
  • Used in traditional Chinese medicine |
| Aromatherapy                      | • Reduced fatigue in a small clinical study when combined with footsoak and reflexology with patients with unspecified cancers250 |
| **Ashwagandha** | • Reduced anxiety and depression up to six weeks in clinical trials of patients, many of which had breast cancer\(^{251}\)  
• Used in the Block program\(^4\)  
  | **Alleviated chemotherapy-induced fatigue and improved quality of life in a small study of breast cancer patients\(^{252}\)**  
  o Used in these programs and protocols:  
    o Alschuler & Gazella complementary approaches\(^3\)  
    o Block program\(^4\)  
    o MacDonald breast cancer program\(^8\)  
    o McKinney protocols\(^9\)  
  • Used in Ayurveda |
| **Black cohosh** | • Improved sleep in postmenopausal women\(^{253}\)  
• Lack of clear evidence of reduced hot flashes in reviews,\(^{254}\) although some studies and analyses have found an effect\(^{255}\)  
• Promoted bone development and showed weak estrogen-like activity on vaginal mucosa in postmenopausal women\(^{256}\)  
• Reduced depression\(^{257}\) and joint pain (in arthritis patients)\(^{258}\)  
• Liver problems are noted, perhaps due to quality and mixing of different species\(^{259}\)  
• Used in the MacDonald breast cancer program\(^8\) |
| **Curcumin** | • Some evidence of reduced severity of radiation dermatitis in breast cancer patients\(^{260}\)  
• Reduced treatment symptoms such as nausea, constipation, diarrhea, weight loss, soreness and ulceration with lecithinized curcumin\(^{261}\)  
• Preliminary clinical evidence of slightly reduced effectiveness of tamoxifen\(^{262}\)  
• Used in these programs and protocols:  
  o Lemole, Mehta & McKee protocols\(^7\)  
  o MacDonald breast cancer program\(^8\)  
• Used in traditional Chinese medicine and Ayurveda |
| **Flaxseed lignans** | • Better mental health among breast cancer patients in observational data\(^{96}\)  
• Ineffective in reducing hot flashes in postmenopausal women, either with or without breast cancer\(^{263}\) |
<table>
<thead>
<tr>
<th>Supplement</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginseng</td>
<td>Notable preclinical evidence: reduced radiation therapy-induced lung damage in cell(^{264}) and animal studies(^{265}) Used in the MacDonald breast cancer program(^{8})</td>
</tr>
<tr>
<td></td>
<td>Improved quality of life in breast cancer patients in epidemiological data(^{106}) Weak evidence of reduced fatigue across illnesses and conditions(^{266}) No significant improvement with cancer-related fatigue, anxiety, depression, symptoms, quality of life and functional scores among patients with advanced cancer(^{267}) Used in the MacDonald breast cancer program(^{8})</td>
</tr>
<tr>
<td>Inositol hexaphosphate</td>
<td>Reduced cytopenia (reduction in mature blood cells), drop in leukocyte and platelet counts with chemotherapy, plus improved quality of life, functional status and ability to perform daily activities(^{268}) Topical application after lumpectomy improved quality of life in breast cancer patients(^{269}) Used in the Block program(^{4})</td>
</tr>
<tr>
<td>Maitake mushroom</td>
<td>Some evidence of improved chemotherapy-related symptoms in patients with advanced breast cancer(^{52}) Used in these programs and protocols: Alschuler &amp; Gazella complementary approaches(^{3}) Block program(^{4}) Used in traditional Chinese medicine</td>
</tr>
<tr>
<td>Melatonin</td>
<td>Improved sleep, fatigue, social and cognitive functioning and quality of life in breast cancer patients(^{97}) Reduced depressive symptoms(^{270}) Improved sleep latency, reduced pre-operative anxiety and prevented agitation(^{271}) Caution on use shortly before surgery as it can magnify the effects of anesthesia(^{4}) Protected normal reproductive cells during chemotherapy(^{272}) Used in these programs and protocols: Block program(^{4}) Lemole, Mehta &amp; McKee protocol(^{7}) MacDonald breast cancer program(^{8})</td>
</tr>
</tbody>
</table>
| **Reishi mushroom** | • May improve fatigue in women with breast cancer\(^{273}\)  
• Improved quality of life\(^{274}\)  
• Notable preclinical evidence: reduced chemotherapy-induced nausea and vomiting in animal studies\(^{275}\)  
• Used in these programs and protocols:  
  o Alschuler & Gazella complementary approaches\(^{3}\)  
  o Block program\(^{4}\)  
  o MacDonald breast cancer program\(^{8}\)  
• Used in traditional Chinese medicine |
| **Selenium** | • Reduced upper limb lymphedema following surgery and radiation treatments\(^{239}\)  
• Used in the MacDonald breast cancer program\(^{8}\) |
| **Shiitake mushroom** | • Improved quality of life when added to immunotherapy in a pilot study\(^{276}\)  
• Improved quality of life in patients receiving chemotherapy in a pilot study\(^{277}\)  
• Used in these programs and protocols:  
  o Alschuler & Gazella complementary approaches\(^{3}\)  
  o Block program\(^{4}\)  
• Used in traditional Chinese medicine |
| **Vitamin and mineral combination (vitamins A, E, C, B, K and D plus calcium, magnesium and trace minerals)** | • Used to prevent treatment-related nutrient deficiency in the Block program\(^{4}\) |
| **Vitamin C** | • Improved quality of life and physical function, and reduced nausea, loss of appetite, fatigue, depression, sleep disorders, constipation, dizziness and bleeding due to chemotherapy and/or radiation therapy [intravenous vitamin C]\(^{278}\)  
• Reduced endocrine therapy-induced hair loss when applied topically\(^{279}\)  
• Used in these programs and protocols:  
  o Block program\(^{4}\)  
  o MacDonald breast cancer program\(^{8}\) |
| **Vitamin E** | • Reduced oral mucositis, hand-foot syndrome and peripheral neuropathy\(^{280}\) |
Some evidence of reduced hot flashes\textsuperscript{281}

Used in the following programs and protocols:
- Chang strategies\textsuperscript{5} for hot flashes
- Lemole, Mehta & Mc Kee protocol\textsuperscript{7}
- MacDonald breast cancer program\textsuperscript{8}

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.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Acetyl-L-carnitine | • Improved signs of heart muscle toxicity during L-carnitine use with doxorubicin treatment in patients with non-Hodgkin lymphoma\textsuperscript{282}  
• No improvement with fatigue\textsuperscript{1}  
• Possible harm from use for peripheral neuropathy\textsuperscript{1}                                                                 |
| Aloe vera       | • Reduced severity of radiation-induced mucositis comparable to benzydamine mouthwash\textsuperscript{283}  
• Reduced incidence of radiation-induced dermatitis in head and neck cancer patients when applied topically,\textsuperscript{284} although an earlier review found both no benefit and and increased risk of dry desquamation (scaly, flaking skin) and pain\textsuperscript{285} |
| Boswellia       | • Reduced radiotherapy skin damage with topical application in a small clinical trial\textsuperscript{286}                                                                                   |
| Chamomile       | • Improved the response to antiemetic drugs to reduce nausea and vomiting during chemotherapy\textsuperscript{287}                                                                 |
| Combination therapies | • Methylphenidate and American ginseng  
  o Reduced fatigue in an uncontrolled retrospective study\textsuperscript{288}  
• Resveratrol, lycopene, vitamin C and anthocyanin  
  o Reduced skin toxicity from external beam radiotherapy in breast cancer patients, including those also undergoing adjuvant chemotherapy with anthracyclines and taxanes\textsuperscript{289}  
• Supplement containing coenzyme Q10 and L-carnitine:  
  o Reduced some indications of fatigue in a small clinical trial of breast cancer patients undergoing chemotherapy\textsuperscript{290} |
<table>
<thead>
<tr>
<th>Supplement</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E, glutamine and acetyl-L-carnitine (About Herbs):</td>
<td>- Reduced incidence and severity of paclitaxel-induced neuropathy&lt;sup&gt;239&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hyaluronic acid cream</td>
<td>- Reduced incidence of high grade radio-epithelitis (overgrowth and inflammation of the mucosal epithelium) when used topically compared to placebo,&lt;sup&gt;291&lt;/sup&gt; but worse acute radiation skin reaction compared to standard treatment&lt;sup&gt;292&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
| Iodine | - Reduced levels of heart distress enzymes (creatinine kinase-MB) during epirubicin chemotherapy<sup>125</sup> See Taking Care of Your Heart below.  
- Reduced fibrocystic breast symptoms<sup>293</sup> |
| L-glutamine | - Reduced duration but not severity of chemotherapy-induced diarrhea<sup>294</sup>  
- Decreased oral mucositis during chemotherapy<sup>295</sup>  
- Reduced incidence and severity of paclitaxel-induced neuropathy<sup>280</sup>  
- Reduced radiation injury in breast cancer patients<sup>296</sup>  
- Cautions surround its role in promoting tumor cell growth and maintenance.<sup>168</sup> |
| Magnolia bark | - Reduced menopausal symptoms, particularly anxiety, irritability and insomnia, when used with E^-Estromineral serena<sup>297</sup>  
- Notable preclinical evidence: protected mouse hearts from doxorubicin-related cardiotoxicity<sup>298</sup> (see also Taking Care of Your Heart below)  
- Used in traditional Chinese medicine and Ayurveda |
| Milk thistle | - Possible use in prevention or treatment of liver dysfunction in patients undergoing anticancer therapy<sup>299</sup>  
- Notable preclinical evidence:  
  o Protected animal heart and liver tissue against doxorubicin-induced toxicity<sup>300</sup> (see also Taking Care of Your Heart below)  
  o Protected and regenerated liver and kidney cells in cell studies<sup>301</sup>  
  o Modestly <em>increased</em> incidence of mammary tumors in rats<sup>302</sup> but not mice<sup>303</sup>  
- Used in the Lemole, Mehta & McKee protocol<sup>7</sup>  
- Used in traditional Chinese medicine and Ayurveda |
A discussion of benefits from dietary intake of omega-3s is in Eating Well above.

- Inhibited bone resorption in breast cancer survivors taking aromatase inhibitors (high-dose EPA)\(^{304}\)
- Reduced paclitaxel-induced peripheral neuropathy in a small clinical study\(^{305}\)
- Improved outcomes, especially body composition, in patients undergoing chemotherapy and/or radiotherapy\(^{306}\)
- Fish oil supplementation improved respiratory muscle strength and endurance, ameliorated functional performance, and kept several blood and plasma concentration at normal levels in a small study of breast cancer patients undergoing chemotherapy.\(^{307}\)
- Reduced weight loss and improved the function of blood neutrophils in patients receiving chemotherapy after surgical tumor (mainly gastrointestinal) removal\(^{308}\)
- May increase resistance to chemotherapy, and so is not recommended on the days surrounding chemotherapy\(^{107}\)
- Used in these programs and protocols:
  - Block program\(^4\)
  - Lemole, Mehta & McKee protocol\(^7\)
  - MacDonald breast cancer program\(^8\)
- Used in traditional Chinese medicine and Ayurveda

Rose geranium in sesame oil nasal spray

- Improved patient-reported nasal symptoms associated with cancer-directed therapy in a small clinical study\(^{309}\)

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allicin</td>
<td>Reduced oxidative damage, cell death (apoptosis) and inflammation in heart tissue from doxorubicin in mice(^{310}) (see also Taking Care of Your Heart below)</td>
</tr>
</tbody>
</table>
| Grape seed extract and/or pycnogenol | Reduced mucositis and intestinal injury from 5-Fluorouracil in mice\(^{311}\)  
|                                 | Ameliorated cytotoxic effects on normal cells/tissues induced by chemo/radiotherapy in animal studies\(^{312}\)  
|                                 | Not effective for preventing breast hardening (induration) following radiotherapy in patients with breast cancer\(^{313}\)  
|                                 | Used in the Lemole, Mehta & McKee protocol\(^7\)  
|                                 | Used in traditional Chinese medicine                                                                |
| Green tea extract              | Reduced cachexia (wasting syndrome) in mice\(^{314}\) and mouse cells\(^{315}\) |
| **Indole-3-carbinol (I3C)** | • Reduced cytotoxicity and cardiotoxicity of doxorubicin in animal studies<sup>316</sup> (see also Taking Care of Your Heart below) |
| **Isothiocyanates** | • Inhibited breast cancer-induced osteolytic bone resorption in animals<sup>317</sup> |
| **Probiotics** | • Reduced weight loss and diarrhea induced by 5-FU and irinotecan in colorectal cancer patients<sup>318</sup> and mice<sup>319</sup>  
• Notable preclinical evidence:  
  o Reduced enteritis (inflammation of the intestine) related to radiation therapy in mice<sup>320</sup>  
  o Reduced oral mucositis and intestinal inflammation from irinotecan<sup>321</sup> and 5-fluorouracil (5-FU) in rats<sup>322</sup> and mice<sup>323</sup>  
• Used in the MacDonald breast cancer program<sup>8</sup> |
| **Resveratrol** | • Reduced doxorubicin-induced cardiotoxicity in preclinical studies<sup>324</sup> (see also Taking Care of Your Heart below) |

**Other therapies with preclinical evidence only for managing side effects and promoting wellness**
- • Quercetin

**Group 6: Evidence of no efficacy or may be dangerous**

<table>
<thead>
<tr>
<th><strong>Therapy</strong></th>
<th><strong>Notes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrazine sulfate</td>
<td>• Ineffective for improving appetite or muscle wasting (cachexia) in cancer patients&lt;sup&gt;325&lt;/sup&gt;</td>
</tr>
<tr>
<td>Soy supplements</td>
<td>• No effect on menopausal symptom scores or quality of life among women with breast cancer having menopausal symptoms&lt;sup&gt;326&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
## 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.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Bisphosphonates, including clodronate and zoledronic acid | • Conclusions from an interdisciplinary expert panel of clinical oncologists and of specialists in metabolic bone diseases:  
  o Benefit with cancer treatment-induced bone loss (CTIBL)  
  o Recommended for patients with metastatic bone disease from breast cancer  
• Prevented bone mineral density loss associated with breast cancer therapy  
• Delayed time to a skeletal-related event and reduced bone pain  
• Require a prescription from a licensed physician  
• Clodronate is currently not approved for use in the US, but is approved in 67 other countries. |

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Chronomodulated therapies | • Reduced grade 2 or higher acute skin reaction to radiation therapy  
• Low toxicity of mitoxantrone, 5-fluorouracil and folinic acid in metastatic breast cancer patients in a preliminary trial  
• "Pivotal" for maintaining rest-activity rhythms and health-related quality of life of breast cancer patients  
• Used in the Block program |
Propranolol and other beta blockers

- Reduced pain and neuropathy and increased weight gain\(^{334}\)
- Reduced emotional distress\(^{335}\)
- Reduced risk of heart failure and markers of cardiotoxicity in patients undergoing anthracycline chemotherapy, especially with carvedilol use\(^{336}\)
- Reduced cardiotoxicity and improved survival in female breast cancer patients undergoing trastuzumab/anthracycline treatment\(^{337}\) (see also Taking Care of Your Heart below)
- Requires a prescription from a licensed physician
- Used in the Lemole, Mehta & McKee stress management protocol\(^7\)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>- Decreased peripheral neuropathy in animal studies(^{338})</td>
</tr>
<tr>
<td></td>
<td>- Decreased cognitive impairment from cisplatin treatment in animal studies(^{339})</td>
</tr>
<tr>
<td></td>
<td>- Requires a prescription from a licensed physician</td>
</tr>
<tr>
<td>Statins</td>
<td>- Reduced cardiotoxicity from the use of anthracycline therapy and doxorubicin in preclinical studies(^{340}) (also see Taking Care of Your Heart below)</td>
</tr>
<tr>
<td></td>
<td>- Associated with serious side effects including permanent muscle damage and impaired cognitive function; their potential benefits in breast cancer must be weighed against the risk, and they should be discontinued promptly if serious side effects occur (see BCCT’s Statins summary)</td>
</tr>
<tr>
<td></td>
<td>- Requires a prescription from a licensed physician</td>
</tr>
</tbody>
</table>

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

**Diets and Metabolic Therapies**

A diet designed to address fatigue in breast cancer survivors showed positive results in a small pilot study.\(^{341}\)

Periodic or short-term fasting may reduce chemotherapy side effects (vomiting, diarrhea, fatigue and weakness).\(^{342}\) Integrative oncologist Dwight McKee, MD, has advised some of his chemotherapy patients to follow intermittent fasting during chemotherapy.
Mind-Body Approaches

Mind-body approaches including music therapy, meditation and yoga have been shown to improve side effects and symptoms as described in these BCCT summaries:

- Mind-body approaches (including music therapy and meditation)
- Yoga

Energy Therapies

Energy therapies with evidence for improving side effects and symptoms include these:

- Healing Touch
- Qigong
- Reiki
- Therapeutic Touch

Manipulative and Body-based Methods

- Acupuncture and acupressure
- Massage,\(^{343}\) perhaps including aromatherapy

Therapies Using Heat, Cold, Sound, Light or Cutting-edge Radiotherapy

- Cryotherapy (cold treatment)
  - Reduced chemotherapy-induced peripheral neuropathy and dysfunction in a small clinical trial\(^{344}\)
  - Used in the Block program\(^{4}\)

Palliative Care

If you have advanced, incurable cancer that has stopped responding to conventional treatment, your oncologist, if pushed, will likely offer you more chemotherapy to try, even when it is unlikely to work and may worsen the quality of your life or even hasten death. This may be a time to push for your physician to be honest and to talk about realistic hope for quality of life, as so much more can be done for you with good palliative care. Furthermore, many patients receiving good palliative care as well as integrative approaches may actually live longer than expected. Such approaches described above include the Block Center for Integrative Cancer Treatment and the Bastyr Integrative Oncology Research Clinic approach.

See BCCT's Palliative Care summary.
Reducing Risk

Reducing the risk of developing cancer or the risk of recurrence

Risk Factors

Generally accepted individual risk factors for breast cancer include these, with varying levels of association:\textsuperscript{345}

- Genetic factors and family history of breast cancer
- Pregnancy history (late age first pregnancy or having no children)
- Menstrual history (early age of puberty or later age of menopause)
- Dense breast tissue
- Chest radiation
- Recent oral contraceptive use
- Combination hormone therapy (see also below)
- Cigarette smoking
- Alcohol consumption

Lifestyle and environment influence the risks of developing breast cancer and of recurrence after treatment.

Hormone Replacement Therapy and Risk

A 2019 meta-analysis found an increased risk of breast cancer with all types of menopausal hormone replacement therapy except vaginally inserted estrogen.\textsuperscript{346} According to coauthor Gillian Reeves, PhD, use of menopausal hormone therapy for 10 years results in about twice the excess breast cancer risk associated with five years of use, but there appears to be little risk from use of menopausal hormone therapy for less than one year, or from topical use of vaginal estrogens that are applied locally as creams or pessaries and are not intended to reach the bloodstream.\textsuperscript{347}

Although these risk factors are important, they do not fully explain why many people develop breast cancer. Lifestyle and environment influence the risks of developing breast cancer and of recurrence after treatment.

From Dr. Ted Schettler’s \textit{The Ecology of Breast Cancer}:\textsuperscript{18} Breast cancer risk factors help shape conditions that foster vulnerability to the disease and less favorable outcomes. Risk factors for which the strength of evidence varies from strong to probable to plausible:

- Certain kinds of diets
- Inadequate physical activity
- Exposures to certain environmental chemicals or contaminants
- Non-ionizing radiation
- Inadequate vitamin D status
It Takes a Village (or a Whole Country) to Reduce the Risk of Breast Cancer

Reducing these risk factors “cannot be accomplished by individuals alone. Public health strategies to re-shape the terrain are essential.” Many of these can only partially be addressed by changes in individual behavior. Multi-level public-health and policy interventions at the population level are also necessary in order to re-design system conditions in more favorable ways.

Dr. Schettler synthesizes the research to 2013 and presents practical measures for individuals, healthcare professionals, public health officials, community planners, businesses, schools, governments and farmers to help reduce the burden of this disease at all levels.

Discussing public-health strategies is beyond the scope of this summary, but we refer readers to Dr. Schettler’s book and to the work of organizations such as the Science and Environmental Health Network and the Collaborative on Health and the Environment.

The role of each of the 7 Healing Practices in reducing the risks of breast cancer development and recurrence is described above. Three further factors—alcohol use, breast feeding and adult body weight—are discussed here.

Alcohol Intake

Alcohol consumption is a recognized risk factor—among those with the strongest evidence—for developing breast cancer.

After diagnosis, some studies show that recurrence is higher in those having more than three or four drinks per week, particularly in postmenopausal women.

The American Institute for Cancer Research states: “For cancer prevention, AICR recommends not to drink alcohol. However, our recommendations recognize that modest amounts of alcohol may have a protective effect on heart disease and type 2 diabetes. If you do drink alcohol, limit your consumption to no more than two drinks a day for men and one drink a day for women. Alcohol appears particularly harmful when combined with smoking.”

An extensive 2018 review and systematic analysis goes even further, recommending no consumption of alcohol: “The level of consumption that minimises health loss is zero.” See BCCT’s Healthy Living summary.
Breastfeeding

Breastfeeding brings many benefits to the mother as well as the infant, including reducing the mother’s risk of breast cancer.352

Many organizations, including the University of Texas MD Anderson Cancer Center, recommend breastfeeding your infant for at least six months, and longer is better.353

Adult Body Weight

In the Nurses’ Health Study, a large, prospective cohort study spanning decades, weight gain after age 18 is associated with higher risk after menopause among women who have never used hormone therapy. Women who had lost more than 10 kilograms (22 pounds) since menopause and maintained their weight loss had a lower risk of breast cancer than women with stable weight since menopause.354 See BCCT’s Healthy Living summary.

Therapies to Reduce Risk

Natural Products

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boswellia</td>
<td>• May help to reduce mammary density, a risk factor for breast cancer, but no direct evidence of reduced occurrence355</td>
</tr>
<tr>
<td></td>
<td>Used in these programs and protocols:</td>
</tr>
<tr>
<td></td>
<td>o Block program4</td>
</tr>
<tr>
<td></td>
<td>o McKinney breast cancer protocol9</td>
</tr>
<tr>
<td></td>
<td>• Used in traditional Chinese medicine and Ayurveda</td>
</tr>
<tr>
<td>Curcumin</td>
<td>• Interfered with breast cancer proliferation in both preclinical and clinical studies356</td>
</tr>
<tr>
<td></td>
<td>• Notable preclinical evidence: indications of suppressed or even regressed tumor growth357</td>
</tr>
<tr>
<td></td>
<td>• Preliminary clinical evidence of slightly reduced effectiveness of tamoxifen at higher doses262 (see Commentary below)</td>
</tr>
<tr>
<td></td>
<td>• Used in these programs and protocols:</td>
</tr>
<tr>
<td></td>
<td>o Alschuler &amp; Gazella complementary approaches3</td>
</tr>
<tr>
<td></td>
<td>o Block program4</td>
</tr>
<tr>
<td></td>
<td>o MacDonald breast cancer program8</td>
</tr>
<tr>
<td></td>
<td>• Used in traditional Chinese medicine and Ayurveda</td>
</tr>
</tbody>
</table>
| Flaxseed lignans | • Associations between flax from combined diet and supplements and decreased risk of primary breast cancer in observational clinical data<sup>96</sup>  
• Used in these programs and protocols:  
  o Alschuler & Gazella complementary approaches<sup>3</sup>  
  o McKinney breast cancer protocol<sup>9</sup>  
• Used in traditional Chinese medicine and Ayurveda |
|----------------|---------------------------------------------------------------|
| Green tea extract / EGCG supplements  
See a discussion of the benefits of drinking green tea in Eating Well above. | • Reduced mammographic density (a risk factor for breast cancer) in younger postmenopausal women (aged 50-55), but not in older women, after taking EGCG supplements for a year<sup>358</sup>  
• Used in the MacDonald breast cancer program<sup>8</sup> |
| Omega-3 fatty acid supplements  
See a discussion of benefits of omega-3s from foods in Eating Well above. | • Higher levels from combined diet and supplements are associated with reduced risks of breast cancer<sup>40</sup>  
• No impact of supplements on breast cancer recurrence and improved overall mortality in patients with early stage breast cancer<sup>28</sup>  
• Used in these programs and protocols:  
  o Alschuler & Gazella complementary approaches<sup>3</sup>  
  o Block program<sup>4</sup>  
  o Chang strategies<sup>5</sup>  
  o Lemole, Mehta & McKee protocols<sup>7</sup>  
  o McKinney breast cancer protocol<sup>9</sup>  
• Used in traditional Chinese medicine and Ayurveda |
| Probiotics | • Reduced risk in case-control studies<sup>359</sup>  
• Used in the Alschuler & Gazella complementary approaches<sup>3</sup>  
• Used in traditional Chinese medicine and Ayurveda |
| Vitamin D supplementation (in doses up to 4000 IU per day for adults) | • Healthy postmenopausal older women with a mean baseline serum 25-hydroxyvitamin D level taking vitamin D<sub>3</sub> and calcium supplements did not show a significantly lower risk of all-type cancer at four years.<sup>360</sup>  
• Reduced <i>in situ</i> breast cancer incidence in postmenopausal women taking calcium and vitamin D supplements<sup>361</sup>  
• Decreased risk of recurrence with ER positive, but not ER negative breast tumors, with post-treatment supplement use<sup>115</sup> |
• Genetic variants may influence the impact of vitamin D status on disease-free survival. Used in these programs and protocols:
  o Alschuler & Gazella complementary approaches
  o Block program
  o MacDonald breast cancer program

Vitamin E
• Some evidence of decreased risk of recurrence
• Used in the Block program

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.

<table>
<thead>
<tr>
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</tr>
</thead>
</table>
| Agaricales mushrooms | • Reduced risk of breast cancer with increased daily intake and frequency of consumption, especially in postmenopausal women
  • Prevented breast cancer cell proliferation
  • Used in traditional Chinese medicine                        |
| Black cohosh       | • Reduced risk of primary breast cancer among postmenopausal women and also risk of recurrence
  • Liver problems are noted, perhaps due to quality and mixing of different species
  • Used in traditional Chinese medicine                        |
| DIM (diindolylmethane) *See a discussion of benefits of consuming cruciferous vegetables rich in DIM and other nutrients in Eating Well above.* | • Reduced risk of breast cancer
  • Affected levels of the tamoxifen metabolite endoxifen in a clinical trial and may reduce the benefit of tamoxifen
| Indole-3-carbinol (I3C) | • Some evidence of reduced risk of breast cancer
  • Used in the Alschuler & Gazella complementary approaches  |
## Vitamin C

- Reduced oxidative stress, but limited and conflicting evidence of reduced breast cancer risk\(^{367}\)
- *Increased* postmenopausal breast cancer risk in women taking supplements who had high vitamin C intake from foods\(^{368}\)
- Fewer recurrences in breast cancer patients using vitamins C and E as well as multivitamins\(^{369}\)
- Some plants used in traditional Chinese medicine are high in vitamin C

## Vitamin K

- Reduced risk of incident and fatal cancer of several types, but not breast, from vitamin K\(_2^{370}\)

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

<table>
<thead>
<tr>
<th>Therapy</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Ashwagandha</td>
<td>• Inhibited cancer development in rodents(^{371})</td>
</tr>
<tr>
<td>Grape seed extract</td>
<td>• Reduced tumor numbers in mice, but dependent on the composition of their diet(^{372})</td>
</tr>
<tr>
<td>Inositol hexaphosphate</td>
<td>• Reduced tumor number, incidence and multiplicity in animal studies, more effectively than a high-fiber diet(^{373})</td>
</tr>
<tr>
<td>Iodine</td>
<td>• Reduced tumor incidence in mice treated with molecular iodine(^{374})</td>
</tr>
<tr>
<td>Isothiocyanates</td>
<td>• Reduced the incidence, number and weight of mammary tumors in animals(^{375})</td>
</tr>
</tbody>
</table>
| Lycopene supplements | • Inhibits invasion, migration and proliferation of human breast cancer cells\(^{376}\)  
*See a discussion of benefits of eating lycopene-rich food in *Eating Well* above.*  
• Suggested increase in all-cause risk of mortality with use after breast cancer diagnosis (based on a small sample size)\(^{377}\) |
| Reishi mushroom | • Chemopreventive against breast cancer\(^{378}\) |
| Resveratrol | • Inhibited claudin-low breast cancer growth in mice\(^{379}\) |
Selenium

- Cancer-preventive benefits with several cancers, including mammary cancer in animals.\textsuperscript{380}

Other therapies with preclinical evidence only for reducing risk

- Alpha-lipoic acid
- Calcium D-glucarate
- Glutathione
- Melatonin
- Quercetin

Group 6: Evidence of no efficacy or may be dangerous

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>High-dose oral vitamin C</td>
<td>Greater risk of breast cancer in a large cohort study.\textsuperscript{381}</td>
</tr>
</tbody>
</table>

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

Group 2: Good clinical evidence of efficacy & safety, limited access
Some may require a prescription, for example.

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| Bisphosphonates, including clodronate and zoledronic acid | - Reduced risk of breast cancer, especially invasive and contralateral breast cancer.\textsuperscript{382}  
- Reduced bone recurrence in postmenopausal patients with nonmetastatic breast cancer.\textsuperscript{175}  
- Use is recommended in a Cancer Care Ontario and American Society of Clinical Oncology clinical practice guideline.\textsuperscript{175}  
- Data are extremely limited for bisphosphonates other than clodronate and zoledronic acid.\textsuperscript{175}  
- Require a prescription from a licensed physician  
- Clodronate is currently not approved for use in the US, but is approved in 67 other countries |
| Metformin                                       | - One large retrospective cohort study found no reduced risk of breast cancer,\textsuperscript{383} but the Women’s Health Initiative clinical trials found reduced risk of invasive breast cancer in postmenopausal women only.\textsuperscript{384} |
Reduced overall cancer incidence\textsuperscript{198}
A trend toward improved recurrence-free survival\textsuperscript{199}
Requires a prescription from a licensed physician

Propranolol and other beta blockers

- Decreased risk of breast cancer-related recurrence among postmenopausal women with early primary triple-negative breast cancer,\textsuperscript{183} but no overall reduced risk of recurrence\textsuperscript{385}
- 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.

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<th>Therapy</th>
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| **Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and COXII inhibitors** | - Reduced breast cancer risk from aspirin and possibly other NSAIDs in some studies\textsuperscript{386} but not all;\textsuperscript{387} one meta-analysis found risk varied by cancer type and menopausal status, with decreased risk of \textit{in situ} breast tumors or hormone receptor-positive tumors and reduced risk in postmenopausal women\textsuperscript{388}
- Decreased risk of distant recurrence and breast cancer death among women living at least one year after a breast cancer diagnosis,\textsuperscript{389} especially among patients with high body mass index (BMI)\textsuperscript{390}
- Reduced recurrence with ketorolac and ibuprofen use\textsuperscript{391}
- No effect of a single dose of intraoperative ketorolac on early recurrences.\textsuperscript{392}
- Caution is advised for those with hypertension or risk factors for gastrointestinal bleeding.
- The US Food and Drug Administration warns that ibuprofen, naproxen and ketorolac increase the risk of having a heart attack or stroke; medical supervision is strongly advised with all NSAIDs.\textsuperscript{214} |
| **Statins** | - Reduced breast cancer risk in some but not all studies\textsuperscript{393}
- Decreased five-year breast cancer recurrence rates with initiation less than three years after diagnosis of early stage breast cancer with lipophilic statins but not hydrophilic statins\textsuperscript{394}
- Associated with serious side effects including permanent muscle damage and impaired cognitive |
function; their potential benefits in breast 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

Diets and Metabolic Therapies

These diet and metabolic therapies are associated with lower risk of breast cancer, as described on the BCCT summaries:
- Mediterranean Diet
- Intermittent fasting: Women with early-stage breast cancer who fasted less than 13 hours each night had an increased risk for breast cancer recurrence compared with those fasting 13 or more hours per night.395

Optimizing Your Terrain

Natural Products

- **Agaricales** mushrooms
  - Increased number of natural killer (NK) cells and other biologic markers in breast cancer patients249
- Curcumin
  - Anti-inflammatory and antioxidant, interfering with known contributors to cancer development396
- DIM (diindolylmethane)
  - Anti-inflammatory effects in lab and animal studies397
- Ginseng (About Herbs)
  - Improved immunology among breast cancer patients when used in combination with red ginseng, lilyturf root, and magnolia vine fruit in a small clinical study398
- Maitake mushroom
  - Modified immune response or functioning in patients with advanced breast, liver, or lung cancer52
  - Decreased inflammation in triple-negative human breast cancer cells52
- Omega-3 fatty acids
  - Anti-inflammatory399
- Reishi mushroom
  - Enhanced immunity in cancer patients127
- Resveratrol
  - Inhibited obesity-associated inflammation in mice379
- Shiitake mushroom
  - Improved natural killer (NK) cell activity and immunosuppressive acidic protein (IAP) levels in patients receiving chemotherapy (preliminary evidence)277
Off-label, Overlooked and Novel Cancer Approaches (ONCAs)

- Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and COXII inhibitors
  - Reduced inflammation, a known driver of tumor growth

Breast Cancer and Surgery

Having breast cancer surgery and possible reconstruction may involve extra consideration and care. Planning ahead to minimize pain or discomfort and reduce the risk of infection can bring a happier experience and better clinical outcome.

Hormone Therapy before Surgery

From medical advocate, breast cancer survivor and BCCT advisor Gwendolyn Stritter, MD

Anti-estrogen therapy, typically started after surgery, prevents breast cancer relapse and death in ER+ cancers. However, some patients do not relapse even if they do not take anti-estrogen medication. Other patients will relapse despite taking them. This means a significant number of patients taking anti-estrogens suffer from the adverse effects of treatment without the benefit of improved outcomes. Taking anti-estrogens before surgery enables your healthcare team to determine if you would respond to such treatment. This can save five to 10 years of ineffective therapy for those who would not respond. Another benefit of neoadjuvant hormone therapy: good outcomes despite less aggressive surgery, such as lumpectomy instead of mastectomy.

It is not surprising that there is a groundswell of support in some centers for giving anti-estrogens before surgery in women with ER+ breast cancer. This allows the patient and the oncology team to know whether a particular medication is effective against the breast cancer and, if it does not induce a partial or complete remission, allows switching to a more active treatment regimen before surgery.

I had tamoxifen before surgery for my ER+ breast cancer, and seeing most of my cancer disappear on MRI over the ensuing 6 months was very gratifying. Knowing the tamoxifen worked so well kept me highly motivated to continue it for the next 5 years.

Breast Reconstruction: Now More Options

Two basic types of breast reconstruction are available after mastectomy:

1. Breast implants
2. Flap reconstruction using tissue from your own body to reconstruct the breast

Further options are available within those two categories. To learn more about the standard post-mastectomy breast reconstruction options, see an online decision aid called BRECONDA: Breast Reconstruction Decision Aid. Note that this aid does not mention prepectoral implants.
Current discussion on implants involves subpectoral expander-based breast reconstruction. For many years, the standard has been to place the implants under the pectoralis major muscle (PMM), partially detaching that muscle. Although this implant position is thought to give a better cosmetic result, many women report problems due to partial injury of the PMM with subsequent muscular deficit, breast animation and postoperative pain.

Evidence supports another way to position breast implants: placing the implant above the PMM and covering it with a dermal matrix derived from pig tissue. The procedure is called prepectoral implant placement and complete coverage with porcine acellular dermal matrix (ADM). Evidence thus far indicates this procedure provides good cosmetic results.\textsuperscript{402} However, the use of ADM has been associated with higher rates of overall complications, seroma (a buildup of fluid where tissue has been removed), infection and reconstructive failure.\textsuperscript{403} You and your surgical team need to assess risks and benefits carefully.

An article in the \textit{New York Times} provides a discussion of this procedure as well as describing Dr. Deborah Cohan’s experience with replacing her sub-pectoral implant with a pre-pectoral implant: New approach to breast reconstruction may reduce pain and weakness for some.

See also Dr. Susan Love's book, \textit{Dr. Susan Love’s Breast Book. 6th edition}, for an in-depth discussion of reconstruction options.

Avoiding Complications After Breast Surgery

Why Is It Important (Besides the Obvious)?

When planning for surgery, several decisions and actions can reduce the risk of postoperative complications. Such complications, while not occurring in the majority of patients, do affect many. These include

- Infection
- Seroma (fluid collection in the surgical area)
- Hematoma (blood collection in the surgical area)
- Reconstructive failure (loss of implant or flap)
- Pain

Of these complications, infection is one for which patient decisions and behaviors have a big impact. Also the type of surgery makes a difference—reconstructive procedures have a much higher complication rate than lumpectomy or simple mastectomy. We will be highlighting ways to avoid infection and the reconstructive techniques that are least prone to complication.

Most people are aware that complications from surgery cause increased hospitalizations and healthcare spending. But many are not aware that they can delay important time-sensitive adjuvant treatment such as chemotherapy or radiotherapy,
resulting in worse survival. Complications also reduce patient satisfaction with the procedure itself and with the cosmetic outcome.

Fortunately, intensive study has found ways to reduce complications. Surgeons and patients now have a lot of information that will help them. First of all, it is important to know whether you or your surgical procedure have specific factors that increase your risks for problems.

Patient Characteristics and Complication Rates

The following patient characteristics and behaviors are associated with higher risk of postoperative complications:

- Obesity, with a body mass index of 30 or higher
- Tobacco smoking
- Age 65 or older
- Hypertension
- Compromised immunity or inflammation
- Hyperglycemia (high blood sugar or poorly controlled diabetes)

Having more than one of these risk factors multiplies the risk of complications. Addressing one or more of these factors before surgery decreases complications. The overall complication rate is 12.6 percent for women older than 65 who choose immediate reconstruction after mastectomy, compared with 6.8 percent for those under 65.

Surgery Characteristics and Complication Rates

Infection rates for breast reconstruction after mastectomy can exceed 30 percent. Postoperative complications are higher in these situations:

- Immediate reconstruction following mastectomy
- Flaps (LD, TRAM or DIEP)
- Bilateral procedures
- Radiation therapy during or after reconstruction
- Chemotherapy

Of note, some institutions will strongly advise delaying reconstruction until after radiation therapy for those who currently smoke simply because performing an immediate breast reconstruction after mastectomy doubles the complication rate.

Neoadjuvent or adjuvant treatments, such as chemotherapy or radiation (given prior to or after surgery) may not only increase the risk for infection but may also cause further tissue damage. If you need these treatments, talk with your doctor about the best timing of reconstructive surgery in relation to other treatments.

Surgical infection rates vary considerably for different types of surgery, for different hospitals, and for different surgeons (or even with the same surgeon as he or she gains experience). Longer hospital stays are also associated with higher infection rates. Information on hospital postoperative infection rates can be found at Medicare.gov—Hospital Compare. Dr. Susan Love advises: "One thing that keeps people in the
hospital after mastectomy is learning how to manage a drain. If possible, ask your
doctor to show you and your family the drain and how to empty it at the pre-op
visit."\textsuperscript{409}

Antibiotic Use and Infection Rates
A systematic review in 2013 found that antibiotic prophylaxis for 24 hours following
breast reconstruction reduced infection rates from 14.4 percent to 5.8 percent. No
further benefit was found for continuing antibiotics past 24 hours.\textsuperscript{410}

Reducing the Risk of Complications: What You and Your Surgeon Can Do

What You Can Do

- First, find out how much time you can take before surgery to develop a plan and
  prepare for surgery.
- Preparing your body
  - Discuss which risk factors you can improve before surgery and come up with
    a plan of actions to take. Actions may include controlling hypertension, stress,
    hyperglycemia and other conditions, or stopping smoking
  - Consider incorporating stress management practices in the weeks leading up
    to surgery. Many patients find imagery practices specific to preparing for
    surgery to be helpful. See BCCT’s Managing Stress, Stress, Mind-Body
    Approaches and Guided Imagery summaries.
  - In addition to effective stress management practices, use emotional support,
    counselling and pre-surgery medication as appropriate to help reduce
    preoperative psychological stress.
  - If you typically clean a cat’s litter box, find someone else to clean it before and
    for several weeks after your surgery.
- Optimizing your surgical context:
  - Check postoperative infection rates for the hospital where your surgery will be
    performed at Medicare.gov—Hospital Compare. While individual surgeon
    complication rates are available for many types of surgery, they are not
    published for breast surgery. Having said that, infection rates tend to be
    higher on average with less-experienced surgeons (a pretty good rule of thumb
    for having good experience is to consider surgeons who have done at least four
    per month of your specific type of surgery for five years).
  - Inform your surgical team of any supplements, herbs or other therapies you’re
    using prior to surgery.
  - If you have financial or social barriers to good pre- and postsurgical care, ask
    to be referred to an oncology social worker or oncology navigator for
    assistance.
  - Work with your surgeon to determine the timing of reconstructive surgery. If
    you’ll be receiving radiation or chemotherapy consider initiating those
    treatments before reconstructive surgery.
  - Schedule your surgery as an ambulatory procedure rather than as an
    inpatient hospital stay if possible.
Discuss your options for anesthesia, post-surgical pain control (see more about ERAS protocols below) and the steps in the column at right with your surgical team at the pre-op visit.

- Immediately before surgery:
  - Avoid presurgical dehydration.
  - See if you can postpone surgery if you develop a cold, flu, pneumonia or other infection shortly before scheduled surgery.

- After surgery
  - Before leaving the hospital, be sure you (and anyone who will be assisting you at home) fully understand and follow all wound care instructions carefully. Call your physician immediately if you show any signs of infection (increasing amount of any of the following: redness, swelling, pain, or discharge from wound).
  - Avoid contact with soil for two or more weeks after surgery.
  - Avoid procedures that might introduce infection to the breast, such as nipple piercing or a tattoo.
  - Consult an integrative physician or licensed naturopath (preferably one who is certified in oncology) to recommend approaches to maintain healthy immune function to improve wound healing and reduce risk of infection.
  - In the weeks following your surgery, if you need a medical procedure that may introduce bacteria to the body, check with your surgeon about using prophylactic antibiotics.

What Your Surgeon Can Do

- Assess all choices and optimize risk factors, including patient characteristics and status of adjuvant therapy, such as radiotherapy and chemotherapy.
- Avoid textured implants due to a possible increased risk of anaplastic large-cell lymphoma.411
- Because half of infections occur more than 30 days after a procedure, implement a plan for follow-up care, including appointments and phone calls.
- Reduce immunosuppression induced by surgery and anesthesia412
  - Use regional anesthesia and IV propofol as primary anesthetic when possible
  - Provide adequate pain control throughout the surgical experience while minimizing the use of opioids (e.g. morphine, oxycodone, codeine).
  - Avoid opioids during or after surgery by using and intravenous propacetamol and anti-inflammatories such as ketorolac while in the hospital and then using oral anti-inflammatories such as ibuprofen or naproxen after discharge.
  - Avoid hypothermia by maintaining core body temperature devices such as fluid warmers and external body warmers.
- Remove catheters and drains as soon as possible.
- Use antibiotic prophylaxis.

Post-surgical Pain Management

According to one national report,413 18 percent of opioid addicts or persistent users got their first opioid prescription after surgery. Evidence also shows that use may increase your risk of cancer recurrence.414 These are both good reasons to carefully consider whether use is necessary.
Fortunately, some hospitals are now discharging even their post-mastectomy patients without any opioids at all and, despite this, are achieving better pain control than with standard treatment that includes opioids. Maimonides Medical Center in Brooklyn, New York, is on the forefront of this movement, as discussed in their 2019 paper, Mastectomy is no longer an indication for postoperative narcotic. Many other hospitals are instituting their own opioid-avoiding protocols. Dr. Stritter strongly recommends that you ask your surgeon at the pre-op visit whether their hospital has a post-mastectomy opioid-sparing ERAS (Enhanced Recovery After Surgery) protocol. While we are in the throes of an opioid epidemic, it makes a lot of sense to minimize unnecessary opioid prescriptions.

In addition to pain control, some retrospective studies suggest that a single intraoperative dose of NSAIDs such as ketorolac may even reduce the risk of breast cancer recurrence. But a single dose may not be enough.

Dr. Stritter, once interested in the idea of using such a protocol for breast cancer surgery, has come to a different conclusion. “The initial reports were based on retrospective, observational studies that had no control group.” Dr. Stritter’s confidence in those reports evaporated when Forget published her updated report—“a definitive prospective, randomized trial—at the 2018 San Antonio symposium that showed no effect of a single dose of intraoperative ketorolac on early recurrences.” Dr. Stritter thinks it doesn’t make physiological sense that a single dose of ketorolac would reduce the chance of recurrence or metastasis. “The healing breast would have the epigenetic, genetic and proteonomic changes of wound healing—a well-documented pro-oncogenic environment—for several weeks until the incision has healed.” That is why after her bilateral mastectomy, Dr Stritter used anti-inflammatories (and no opioids) during her entire post-operative period, not only for pain relief but in hopes of creating an anti-oncogenic tumor microenvironment.

A 2018 review of anesthetic interventions in breast cancer concluded that “based on the available evidence, an ideal anesthetic in this patient population would involve a combination of TIVA (propofol), regional anesthesia (paravertebral block), non opioid sedatives (clonidine or dexmedetomidine), and COX-2 inhibition (ketorolac).”

Non-drug measures that can reduce inflammation, pain and opioid use:

- Acupuncture
- Options with less published evidence regarding effectiveness.
  - Electroacupuncture and transcutaneous electrical acupoint stimulation (TEAS)
  - Transcutaneous electrical nerve stimulation (TENS)
  - Pulsed electromagnetic fields in most but not in all studies
Dr. Stritter's Approach

Dr. Gwen Stritter, MD, medical advocate and board-certified anesthesiologist, had bilateral mastectomy for breast cancer. She followed this approach, without opioids, to achieve good pain control and speedy recovery after her 2014 surgery:
- Before incision: IV ketorolac, 30 mg; bilateral paravertebral blocks
- During surgery: no opioids; no nitrous oxide; lots of IV propofol
- Post-operatively:
  - Ibuprofen 800 mg every 8 hours around the clock
  - Omeprazole 20 mg twice a day to avoid the gastrointestinal issues
  - After about five or six days, started to get a lot of edema from the ibuprofen so stopped ibuprofen and omeprazole; switched to boswellia and curcumin

Reducing the Risk of Chronic Pain after Mastectomy or Breast Reconstruction

From medical advocate, breast cancer survivor and BCCT advisor Gwendolyn Stritter, MD

About 15 to 20 percent of patients have moderate to severe chronic pain after breast cancer surgery. Regional anesthesia (also known as nerve blocks) has been shown to reduce the risk of persistent pain after breast surgery. Thoracic paravertebral blocks and PECS blocks are the two types of regional anesthesia most widely used.

Performing such nerve blocks before surgical incision allows for “light” general anesthesia (such as primarily using IV propofol instead of inhaled gases). This in turn results in quickly “waking up” from anesthesia without nausea or prolonged grogginess. Enough evidence shows that regional anesthesia lowers the chance of subsequent relapse and metastasis. A formal clinical trial is looking at this very issue: Regional Anesthesia and Breast Cancer Recurrence.

Not all anesthesiologists have the training or experience to do these blocks well. An appointment with the anesthesia team well in advance of surgery will increase the odds of getting these blocks before mastectomy. I had bilateral paravertebral blocks for my double mastectomy and required only oral anti-inflammatory medication for post-op pain control. My experience was documented in this video: Gwen Stritter's Painless Double Mastectomy.

Infection Response

Despite our best efforts, we can sometimes still get an infection after breast surgery. Fortunately, it is uncommon for a mild infection to cause a significant worsening of outcomes. But knowing what to do (and what not to do) will help prevent a mild infection from becoming a serious one.
What if you do get an infection:

- Report symptoms of infection immediately to your surgeon and begin treatment promptly. If antibiotics are prescribed, take as directed.
- Eat well to maintain a healthy nutritional state. Consider consulting a board-certified oncology dietician for specific dietary recommendations.
- If antibiotics are prescribed, eat well and follow other practices to restore a healthy microorganism balance. See Eating Well, Mediterranean Diet and Your Microbiome.
- Consider consulting an integrative oncology specialist about additional measures to clear infection, help wound healing, control inflammation and minimize tissue fibrosis (scarring) from surgical wounds and/or from radiation therapy.

Recovery and Remission Maintenance

BCCT does not recommend any particular remission maintenance approach. The strategies provided here are supported by evidence of improved outcomes.

Balancing Terrain

Several imbalances in your terrain can make the body more susceptible to infection, slower to heal wounds and/or more hospitable to cancer. Chronic inflammation, insulin resistance/glycemia, obesity and imbalanced stress chemistry may be particularly important to balance in relation to surgery, wound healing and reducing recurrence risk. For more information, see BCCT's Body Terrain and the Tumor Microenvironment summary.

In his book Life over Cancer: The Block Center Program for Integrative Cancer Care, Keith Block, MD, lists glycemia, stress chemistry/biorhythms and inflammation as terrain factors common in breast cancer. Compromised immunity such as from chemotherapy, surgery, anesthesia or opioid use may also increase the risk for infection and recovery. Approaches to address these factors involve healthy lifestyle practices, such as the 7 Healing Practices. You can learn more about Dr. Block’s integrative program to address these terrain factors in his book:

- Chapter 15, Inflammation: Overcoming cancer’s fiery side
- Chapter 16, Immune Surveillance: Mounting the immune barricades
- Chapter 18, Glycemia: Breaking cancer’s sugar addiction

In their books, Lise Alschuler, ND, FABNO, and Karolyin Gazella list five key body pathways to target to make your body inhospitable to cancer. Three of those pathways most relevant to preventing and managing surgical complications are the immune system, insulin resistance and inflammation. See the following chapters:

- The Definitive Guide to Thriving after Cancer: Chapters 1-5
- The Definitive Guide to Cancer, 3rd Edition: An Integrative Approach to Prevention, Treatment, and Healing:
  - Chapter 8, Immune system (including stress management)
  - Chapter 9, Inflammation
  - Chapter 11, Insulin resistance
Alschuler and Gazella also devote a portion of chapters 6 and 7 to integrative approaches to preparing for, mitigating side effects from and enhancing outcomes of cancer surgery.

The Breast Cancer Companion: A Complementary Care Manual: Third Edition by Barbara MacDonald, ND, FABNO, is an excellent guide for oncology naturopaths caring for those with breast cancer. She provides guidance on natural approaches to consider across the spectrum of breast cancer: reducing inflammation; support through surgery, including wound healing; preventing recurrence and monitoring after conventional treatment is completed. See these sections in particular:
- Chapter 1, section 2.1.4, Inflammation
- Chapter 2, section 2, Diagnostic Tests and Surveillance Tests
- Chapter 4, Preparing for Surgery
- Chapter 9:
  - Section 3, Monitoring while in Remission
  - Section 5, Recurrence Prevention Strategies
  - Section 6, Classical Naturopathic Treatment of Breast Cancer Survivors
  - Section 7, Post-treatment Laboratory Testing

Post-treatment Monitoring

When you have finished treatment, discuss and develop a survivorship plan with your cancer treatment team. Your survivorship plan includes instructions and a schedule for follow-up visits, plus testing and guidance on lifestyle and other self-care practices to help you recover and prevent recurrence. The type of testing and monitoring done to assess your response to treatment and pick up on recurrence depend on your specific cancer, treatment and risk for recurrence.

You need to find a balance in monitoring for breast cancer recurrence. Talk with your oncologist about your risk of recurrence and the type and frequency of monitoring best for you. Based on your risk, ask these questions:
- Have we done everything we know to do from a treatment standpoint to treat the breast cancer?
- What type and frequency of monitoring is best for me?
- What are the available monitoring tests and tools?

Valid and reliable tests to pick up on recurrence early are under development. Blood tests such as circulating tumor DNA (ctDNA) and circulating tumor cell testing (CTC) have generated a lot of excitement, but they’re not yet ready for routine clinical use. According to Dr. Stritter, two fairly well-validated ctDNA tests, Guardant 360 and FoundationOne Liquid, are used to monitor treatment response in metastatic breast cancer. She suspects that within the next couple of years these tests may be validated for use in the post-primary/adjuvant, NED (no evidence of disease) setting as a very early warning of impending recurrence. BCCT is monitoring this situation and will update this page when new developments are announced.

Meanwhile, some women with no evidence of disease but at high risk of recurrence have requested ctDNA testing, understanding that insurance is not likely to pay for
the tests. Guardant 360 will accept samples only in the case of metastatic breast cancer. Foundation Medicine’s ctDNA test costs about $5800, and—except for metastatic disease—insurance usually won’t cover the costs. Fortunately, Foundation Medicine, and perhaps other companies, do not charge the patient if the test does not reveal any ctDNA. Further, Foundation Medicine and other companies offer financial aid and discount programs in some cases.

For more information on testing see Standard and Non-standard Diagnostic Approaches. Other surveillance tools currently employed with those at increased risk of recurrence are listed on BreastCancer.org’s site: Blood Marker Tests.

**DCIS Treatment**

From medical advocate, breast cancer survivor and BCCT advisor Gwendolyn Stritter, MD

**De-escalation of DCIS Treatment**

60 percent of the patients with DCIS would not progress to invasive breast cancer even without any treatment whatsoever. But not knowing which patient will progress, combined with the potential for metastasis in those who do progress, has understandably led oncologists to overtreat everyone in the hopes of improving the survival of the 40 percent who are at risk.

Fortunately, this is beginning to change as researchers are steadily showing ways to reduce DCIS treatment while maintaining excellent outcomes. Radiation therapy is a good example. Radiation therapy decreases relapse rates for DCIS, but it does not improve survival. For some patients, the reduction in relapse outweighs other considerations and they opt for radiation therapy. Now with the advent of genomic testing, oncologists are now actively researching tests such as Oncotype DX DCIS\(^{126}\) and SweDCIS\(^{427}\) that help limit radiation therapy only to those would have a high risk of relapse without it.

Preliminary data also show that even surgery can be avoided in low-risk DCIS. This research is compelling enough that an ongoing 50-state clinical trial of active surveillance vs. surgery in underway: Comparison of Operative to Monitoring and Endocrine Therapy (COMET) Trial For Low Risk DCIS (COMET).

It is very exciting to see the breast oncology field moving in the direction where surgery and radiation therapy are used only on the few patients who need them.\(^{428}\)

**Low-dose Tamoxifen and DCIS**

It turns out that the dose of tamoxifen you are taking may be much higher than needed. This research figured prominently at the December 2018 San Antonio Breast Cancer Symposium—for good reason. It was recently published in the *Journal of Clinical Oncology.*\(^{429}\)
First, some background. Conventional medical research, especially cancer research, has a notable deficiency: a strong tendency to test only the “maximally tolerated dose” of any given research drug. This approach is lots cheaper and lots easier than testing two to four other doses to find the sweet spot (maximal effectiveness, minimal side effects). Accordingly, it has been known for quite a while that the standard dose of tamoxifen—20 mg—may be much higher than that necessary to prevent non-invasive breast “pre-cancers” such as DCIS, LCIS and atypical ductal hyperplasia (ADH) from progressing to invasive breast cancer.

A group in Italy randomized 500 women with non-invasive breast disease to take either 5 mg tamoxifen per day or none at all (placebo group) over the course of three years. They found the decrease in DCIS/LCIS recurrence and that of invasive breast cancer in the low-dose tamoxifen group to be equivalent to what we typically see with the 20 mg dose. They also saw a decrease in new breast cancers/pre-cancers in the other breast. But equally important, the risk of blood clotting and endometrial cancer was indistinguishable from that of the placebo group. Here’s the icing on the cake: the incidence of hot flashes and vaginal symptoms (dryness, pain during sex) was minimally increased over the placebo group.\^429

What’s not to love? Equal effectiveness and decreased side effects! But here are some cautions. This is a relatively small study that followed women to an average of only five years. So this protocol is not quite ready for prime time.

Having said that, here are the situations in which you should consider asking your oncologist about low-dose tamoxifen:

- You have LCIS, ADH or ER+ DCIS, and
- You are at higher risk for endometrial cancer, or
- You are at higher risk for blood clotting, or
- Because of intolerable side effects you plan to stop the tamoxifen 20 mg dose thereby increasing your risk of relapse or invasive breast cancer.

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**Taking Care of Your Heart: Cardiac Toxicity and Breast Cancer Treatment**

With contributions from BCCT Advisor Jen Green, ND, FABNO

Caring for your heart is an important part of your wellness plan. According to a 2018 review, following diagnosis, 35 percent of deaths in breast cancer patients are related not to breast cancer, but to cardiovascular disease.\^121

People with breast cancer who are undergoing chemotherapy such as anthracyclines (including Adriamycin/doxorubicin), targeted agents such as Herceptin/trastuzumab, and radiation therapy to the chest are at risk for heart damage. Risk is even higher for those receiving anthracyclines plus Herceptin or anthracyclines plus chest radiation.
As part of your treatment, you may be given toxic drugs and/or radiation therapy to kill cancer cells. The normal cells in and around your heart can also be killed, resulting in cardiac toxicity. Besides cell death, other types of cardiac toxicity can result from cancer treatment:

- Cardiomyopathy
- Myocarditis
- Pericarditis
- Acute coronary syndromes
- Congestive heart failure

With people living longer after their cancer diagnosis and treatment than in the past, this problem is becoming more prevalent, so much so that a new cancer subspecialty—cardio-oncology—has developed. Many cancer treatment centers have cardio-oncology programs.

From a conventional treatment standpoint, preventing heart problems from cancer treatment involves a baseline test of heart function, monitoring those at risk for problems, and adjusting drug dosage and/or frequency or even changing to a less cardiotoxic drug. Radiation oncology is becoming more and more adept at targeting the cancerous tissue and shielding the heart and lungs. Early treatment of heart problems is more likely to prevent serious damage.

The first step is to get a baseline test of heart function (usually an echocardiogram, or ECG), and repeat this testing during treatment if you are at risk for heart problems. Repeat testing four and 10 years after treatment with doxorubicin. Survivors of childhood cancer should have an echocardiogram every one to five years ongoing and during late-stage pregnancy.

An echocardiogram should be taken periodically during treatment—every three months during treatment with Herceptin/trastuzumab, according to guidelines from the American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging and European Society for Medical Oncology. An “echo” takes pictures of the heart and measures the strength of the heart/ejection fraction. Ejection fraction over 55 percent is normal, a mildly weak heart is at 45 to 55 percent, a moderately weak heart is 30 to 45 percent, and below 30 percent is considered severely weakened.

“Heart Healthy” Lifestyle Choices

Some complementary therapies may be helpful, starting with “heart healthy” lifestyle choices including the 7 Healing Practices of eating well, moving more, managing stress and sharing love and support (see also the descriptions above).

Lifestyle practices are the first steps to get your cardiovascular system in the best shape possible, before treatment if possible but also as part of your survivorship plan for health.
A clinical trial of an exercise intervention in breast cancer patients found good evidence of benefit: “Our findings strongly support that tailored exercise training during adjuvant breast cancer treatment may counteract a decline in cardiovascular function, and in particular among those receiving chemotherapy.”  

Be sure to consult with your doctor before starting an exercise program, particularly if you already have heart or other problems such as neuropathy that may require adjustments to a fitness plan. In this case, a cardiac or cancer rehab program may guide you in choosing safe exercise and movement therapies.

Other foundations for protecting your heart during treatment:
- Quit smoking
- Optimize your body weight
- Avoid drugs that stress the heart
  - Cocaine
  - Diet pills
  - Ephedra/ma huang
  - Performance-enhancing drugs
  - Caffeinated energy drinks

Natural Therapies Protective during Adriamycin/Doxorubicin Treatment

Studies on herbs or natural supplements show how these have helped reduce heart damage from Adriamycin/doxorubicin. Please connect with an integrative oncology professional or naturopathic physician for specific guidance. Also see Quality and Sources of Herbs, Supplements and Other Natural Products on the BCCT website.

**Milk thistle**: In a controlled trial, cancer survivors who took milk thistle during doxorubicin treatment had better heart function compared to placebo. Study authors concluded that silymarin “can be recommended as adjuvant drug in patients with ALL under doxorubicin therapy.” Silymarin, a main component of milk thistle, protected animal heart and liver tissue against doxorubicin-induced toxicity. An earlier trial showed that milk thistle is safe to combine with chemotherapy.

**Coenzyme Q10 (CoQ10)**: In a controlled trial, CoQ10 use with doxorubicin preserved heart function. In another small controlled trial in Japan, CoQ10 use during doxorubicin and radiation treatment preserved heart function. Researchers hypothesize that CoQ10 prevents doxorubicin from binding to heart muscle cells. Animal studies also show that CoQ10 supplementation improves the functional and structural integrity of the myocardium during doxorubicin treatment.

Before taking coQ10, consult with your doctor. Because CoQ10 is an antioxidant, it may theoretically interfere with some chemotherapy drugs (such as anthracyclines and cyclophosphamide) or radiation therapy. “Recent in-vitro [cell] studies, however, have shown that CoQ10 does not affect the antineoplastic properties of doxorubicin.”
**L-carnitine:** Many people who have low carnitine from chemotherapy will have weakness in large muscle groups, which can make your legs feel like jello when you walk up the stairs. L-carnitine is established as improving heart function following a heart attack. In a meta-analysis, use of L-carnitine after heart attack was associated with a 27 percent lower risk of dying and 65 percent lower risk of irregular heart rate. In a randomized controlled trial of cancer patients, L-carnitine during doxorubicin treatment improved signs of heart muscle toxicity. Young cancer survivors who received doxorubicin have lower plasma carnitine levels than controls, so L-carnitine has been suggested as a way to prevent heart damage.

Animal studies also show that L-carnitine supplementation improves the functional and structural integrity of the myocardium during doxorubicin treatment.

**Ginkgo:** In a controlled trial in China, people who took Gingold during doxorubicin treatment had fewer abnormal echocardiograms compared to doxorubicin alone. Because ginkgo does not affect how most medicines are metabolized, it appears to be safe to combine with chemotherapy, tamoxifen, anastrozole or letrozole. Ginkgo added to aspirin (either 325 mg or 500 mg) did not affect bleeding risk.

**Arginine:** In a controlled trial, people who took arginine along with doxorubicin had less shortness of breath, palpitations, and fewer ECG changes.

**Iodine:** In a randomized pilot study, women who took iodine during epirubicin chemotherapy for breast cancer had significantly lower levels of heart distress enzymes (creatine kinase-MB) than those taking a placebo.

Natural Therapies Protective during Treatment with Herceptin/Trastuzumab, Perjeta/Pertuzumab or Kadcyla/Trastuzumab Emtansine

Studies of these herbs or natural supplements show improvements in heart strength/ejection fraction. These may be useful if heart strength is reduced from Herceptin or Kadcyla treatment. Please connect with an integrative oncology professional or naturopathic physician for specific guidance. Also see Quality and Sources of Herbs, Supplements and Other Natural Products on the BCCT website.

**Hawthorn berry/crataegus:** In a meta-analysis, hawthorne berry improved heart strength/ejection fraction and symptoms of congestive heart failure.

**L-carnitine:** In a meta-analysis, L-carnitine improved heart strength/ejection fraction and symptoms of congestive heart failure.

**Taurine:** In double-blind, randomized, controlled trials, taurine improved heart function and signs of congestive heart failure.
**Combination of taurine, CoQ10 and L-carnitine:** In a double blind randomized controlled trial, patients who took 3 g taurine, 3 g carnitine and 150 mg CoQ10 had better heart function.\(^{455}\)

**Astragalus:** In a randomized controlled trial, astragalus improved heart strength/ejection fraction.\(^{456}\)

**Berberine:** In a randomized controlled trial, berberine improved heart strength/ejection fraction, ability to exercise, symptoms of congestive heart failure, and heartbeat regularity/ventricular premature complexes.\(^{457}\) Dr. Barbara MacDonald recommends against taking berberine during taxol treatment.\(^{8}\)

**Magnesium:** In a double blind randomized controlled trial, people with severe congestive heart failure who took magnesium had better symptoms and survival.\(^{458}\)

A heart-support protocol developed by Michael Walker, ND, FABNO, includes magnesium (About Herbs), CoQ10, L-carnitine, fish oil, and exercise that can improve heart function that drops during treatment with Herceptin/trastuzumab or Perjeta/pertuzumab.

**Commentary**

BCCT advisor **Gwen Stritter, MD**, February 1, 2019: As a breast cancer medical advocate, I find there are certain areas that patients are really grateful to learn about. I have included a few in sections above: hormone therapy before surgery, regional anesthesia for mastectomy and de-escalation of DCIS treatment.

BCCT advisors **Gwen Stritter, MD, and Jen Green, ND, FABNO**, May 9, 2019: Impact of curcumin on tamoxifen effectiveness

Many are aware that tamoxifen is what we call a pro-drug. A pro-drug is ineffective until specific enzymes in your body activate it. Tamoxifen is metabolized to endoxifen, the effective drug that prevents ER+ breast cancer patients from relapse.

An enzyme called CYP2D6 is responsible for the magic that changes tamoxifen to endoxifen. The activity of this enzyme varies from individual to individual. Part of the variance is due to genetics—some people are born with hyperactive CYP2D6; others have an enzyme that is very sluggish. Many medications—antidepressants like fluoxetine (Prozac), paroxetine (Paxil) and citalopram (Celexa) amongst a host of others—as well as assorted foods and dietary supplements can either activate or slow down CYP2D6.

When this information first started causing a stir in the breast cancer world roughly 10 years ago, researchers hypothesized that taking tamoxifen with a CYP2D6 inhibitor would cause a increase in breast cancer relapse. As it turned out, further clinical research did not bolster this theory,\(^{459}\) leading to a new one: genetics, drugs and dietary intake have complex interactions with the body’s enzyme system. They activate
some enzymes and inhibit others. This results in a variable net effect on the concentration of important drugs. In a 2016 study, the cause of low endoxifen levels could not be identified over 50 percent of the time.\textsuperscript{460}

Because such a complex system is difficult to study, researchers turned away from looking at just CYP2D6 and are focusing on the endoxifen level itself (ignoring the middleman). In one study, researchers in the Netherlands gave tamoxifen with or without curcumin 1200 mg three times a day. The group taking tamoxifen in combination with curcumin had about an 8 percent decrease in endoxifen levels. If the curcumin was compounded with piperine (often done to substantially improve curcumin absorption), endoxifen levels were further decreased by 12 percent.\textsuperscript{262}

Although an 8 to 12 percent reduction doesn’t seem like much, if your genetics and/or dietary habits result in levels of endoxifen just barely in the effective range, the addition of curcumin, and especially with piperidine, could tip the scales in favor of breast cancer growth. The authors of this paper conclude: “co-treatment with curcumin could lower endoxifen concentrations below the threshold for efficacy (potentially 20 to 40 percent of the patients).”

Do keep in mind that this was a very small study, only 16 patients. However, these results are in line with previous lab and animal research so should not be discounted. On the other hand, curcumin supplementation has documented beneficial effects: decreased depression,\textsuperscript{461} anti-inflammatory effects\textsuperscript{462} and lowered cholesterol,\textsuperscript{463} to name a few.

The bottom line: if you are taking curcumin with tamoxifen, ask your integrative practitioner if s/he could substitute another supplement. If not, then request to have your endoxifen levels checked, both before and a month after starting curcumin. Quest Diagnostics, a very reputable lab, offers a “tamoxifen and metabolites” blood test.

BCCT advisor \textbf{Lise Alschuler, ND, FABNO}, August 9, 2018: There are instances when I use specific mushrooms, for instance: \textit{Coriolus} (or \textit{Trametes} \textit{versicolor}) (turkey tail) for breast cancer, \textit{Agaricus blazei} for ovarian cancer and chaga mushroom for melanoma. However, it is a very valuable and reasonable strategy to use a blend that includes mushrooms, each of which is standardized to its polysaccharides and beta-glucans. The key is to use a hot water extract of the fruiting bodies or a full-spectrum extract (includes mycelium) that clearly identifies on its label the quantity of mushroom extract.

Some blends that I often recommend:

Per capsule:

- \textit{Trametes versicolor} (turkey tail) (40% polysaccharides, 40% beta-glucans) - 100mg
- \textit{Grifola frondosa} (maitake) 40% polysaccharides, 30% beta-glucans - 100mg
- \textit{Ganoderma lucidum} (reishi), 40% polysaccharides, 15% beta-glucans - 100mg
- \textit{Lentinula edodes} (shiitake), 409% polysaccharides, 40% beta-glucans - 100mg
I would recommend between 2-3 capsules twice daily.

When recommending single mushrooms, it is important to know how much beta-glucan is in each serving so that I can titrate my dose accordingly. For instance, I often use *Grifola frondosa* (maitake) mushroom to increase white blood cell counts. One product I use contains:

Per 6 tablets:
- Maitake (*Grifola frondosa*) Fruiting body powder - 600mg
- Maitake fruiting body extract, standardized to contain 30% D-fraction - 240mg (so 72mg D-fraction beta glucan)
- Vitamin C 120mg (supports bioactivity)

Cost-permitting, in most clinical studies, the daily dose of mushroom extracts that is correlated with improved survival (especially in breast, colorectal, gastric cancers) is 3000mg/day.

Mushrooms do pack a punch! From a meta-analysis on *Coriolus versicolor* mushroom extracts in patients diagnosed with cancer:
- Over all cancers, there was a 9% absolute reduction in 5-year mortality (one additional patient alive for every 11 pts treated).
- Effects were more evident for breast, gastric or colorectal cancer versus esophageal or nasopharyngeal.

BCCT advisor **Keith Block, MD**, advises patients on heart-damaging medications to take 200 mg or even considerably more of CoQ10 per day. Many heart patients are also on statins. Block says, “Because statins deplete coenzyme Q10 from your muscle cells, particularly your heart, I advise patients on statins to take at least 30 mg of coQ10 per day.”

BCCT advisor **Ted Schettler, MD**, March 4, 2019: Lavender oil (as with some other essential oils) has estrogenic properties at some concentrations. It might be wise to avoid skin application of lavender oil in the setting of an estrogen positive breast cancer diagnosis.

Written by Laura Pole, RN, MSN, OCNS; Nancy Hepp, MS; and Michael Lerner, PhD. Reviewed by Ted Schettler, MD, MPH; and Gwendolyn Stritter, MD; most recent update on October 3, 2019.
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