Empowering Cancer Patients Using Integrative Medicine:

A Novel Model for Breast Cancer Risk Modification

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The Outer Banks Hospital (TOBH) is a small critical access hospital with a two-time commendation level Commission on Cancer (CoC)-accredited program in Nags Head, N.C. The town of Nags Head is located on the Outer Banks, a series of barrier islands off the shore of North Carolina. A popular beach vacation destination, the Outer Banks sees seasonal shifts in its population. During the off-season, the hospital primarily serves a demographic that often reflects common rural disparities, such as disproportionately high percentages of advanced stages of cancer presentation and patients with complex socioeconomic needs. As a CoC-accredited critical access hospital—one of only about a dozen nationwide—TOBH has developed a quality program with a focus on removing rurally linked barriers to care.

Breast cancer is the most common cancer in eastern North Carolina, as well as nationally. Because it is so common, our team repeatedly looks at ways to create innovative approaches to improve breast care locally and favorably impact community outcomes. The hospital's quality improvement (QI) models are simple, and other community hospitals can easily replicate them.

In 2018, TOBH completed an analysis of the many known risk factors for breast cancer within its rural population to see if an opportunity existed to remove disparity as part of a QI project. The analysis was conducted with acknowledgment that some risk factors for cancer are inherently biological, genetically determined, and difficult to change and that many risk factors are biological, environmentally influenced, and *sometimes modifiable*. Examples of the former include family history, ethnic ancestry, breast density, age of menarche, height, and age of menopause. Examples of the latter include BMI (body mass index), exercise, diet, stress and anxiety, use of and timing of hormone replacement therapy, alcohol consumption, and smoking. Our study examined existing patients with breast cancer for most known common biological risk factors, and we used this information to create a two-step process to:

> All patients with newly diagnosed breast cancer are now evaluated prospectively for genetic counseling and testing locally at our hospital based on national guidelines for hereditary breast cancer.[1]

Although the underlying mechanisms of the cancers may be different—mostly hormone related in post-menopausal women and inflammatory mediated in pre-menopausal women—they potentially provide a common denominator for customized intervention through a risk modification model.

1. Model the management of all breast care within the region through risk stratification.
2. Help create care pathways to mitigate the risks wherever possible.

This article summarizes how this rural hospital leveraged integrative medicine with oncology to develop a risk assessment and risk modification model and highlights its early outcomes to mitigate some of the rurally linked disparities in cancer as they pertain to breast care.

Our Quantitative Risk Factor Analysis

To satisfy CoC Standard 4.7, TOBH conducted a multi-year quality study that looked at collective risk factors for breast cancer occurrence based on some unusual observed patterns in local demographics. Our radiation oncologist and Cancer Committee chairman observed a seemingly higher-than-expected prevalence of familial clustering of breast (and linked ovarian and pancreatic) cancers regionally, higher local obesity rates, and an excess of other cumulative above-average risks for breast cancer within our rural population, at least within the existing population of locally treated breast cancer patients. These observations suggested a need to further examine these risk factors and identify any other risks collectively. The hope was that an extensive analysis of known risk factors in existing patients with cancer would reveal patterns that would allow customization of treatments through risk reduction and possibly allow broader modeling of this rural risk in the larger cancer-free population as prevention.

Indeed, further data analysis revealed a remarkably high clustering of breast cancers within families in our demographic area. This finding suggested a need to consider more proactive genetics evaluation, which we incorporated into our cancer program. All patients with newly diagnosed breast cancer are now evaluated prospectively for genetic counseling and testing locally at our hospital based on national guidelines for hereditary breast cancer.[1] Four years of data analysis reveal that 55 percent of patients presenting with breast cancer to our hospital have positive family histories that reveal close (first- or second-degree) relatives with breast or ovarian cancer. Many of these families include at least one first-degree relative, and often at early ages (<50), and 6 percent of patient families report more than one first-degree relative with breast or ovarian cancer. These numbers are roughly four times the comparable percentages seen in large population studies where the majority (75 to 85 percent) of patients with breast cancer studied in larger populations nationally have *no* family history of breast cancer.[2] These flipped familial clustering patterns observed within our region versus elsewhere might suggest a high rural prevalence AND:

- Known inheritable genetic mutations (e.g., BRCA1 or 2) for which patients can be tested OR
- As-yet undiscovered genetic mutations, which likely are not very penetrant in a population and therefore perhaps not as relevant OR
- Shared environmental risk factors clustering within families (e.g., poor diet, common environmental exposures).

Results from our quality study also confirmed high rates of obesity within our rural population of breast cancer patients (~38 percent are obese; 32 percent are overweight, 70 percent have BMI > 25). High rates of obesity (BMI > 30), especially in post-menopausal women, have been shown to consistently increase breast cancer rates due to excess estrogens.[3] It is no surprise that the median age of women with breast cancer at TOBH is 63 (same as nationally), and 87 percent of breast cancers in our community are hormone receptor (ER) positive. Obesity may also be a shared environmental risk factor linked to rural socioeconomics. Additionally, obesity in premenopausal women may correlate with the genesis of triple-negative breast cancers.[4] Although the underlying mechanisms of the cancers may be different—mostly hormone related in post-menopausal women and inflammatory mediated in pre-menopausal women—they potentially provide a common denominator for customized intervention through a risk modification model.

As mentioned previously, due to the observed high rates of familial clustering of breast cancer (55 percent of patients have known family history of same cancers), our hospital cancer program has become very proactive in testing for genetic mutations. We currently test 100 percent of consenting patients ourselves using a genetics extender model. Yet, our three-year broad-panel gene testing results indicate that only 6 percent of patients with breast cancer have true identifiable pathogenic mutations linked directly to their breast cancer (including BRCA, PTEN, CHEK2, CDH1, ATM, RAD51C, etc.).[5] These data suggest that the majority (>90 percent) of familial clustering within the rural area we serve may be due to other low-risk, yet to be identified genetic (polygenic) mutations or, more likely, represent epigenetic-linked somatic events that led to genomic instability in the cells. Examples of such precipitating events include potential carcinogens in the diet or environment, previous radiation exposures, alcohol and tobacco use, or lifestyle (and health) modifiers of our epigenome. Examples of the latter include obesity, type II diabetes mellitus and circulating high levels of insulin, lack of exercise, poor diet, inferior cardiovascular disease, stress, and sleep patterns.

Regardless of the underlying mechanisms, TOBH's cancer patient data indicated a high-risk population rurally with clearly identifiable risk factors and an opportunity for novel intervention by our cancer program.

Our Nature+Nurture QI Approach

Robin Hearne, RN, MS, director of Cancer Services for TOBH, first suggested a novel blended approach to address the care of the whole patient with cancer. With experience in quality care and research, Hearne brings a combined interest in both conventional therapy as a nurse and integrative approaches to cancer care. She completed an integrative medicine leadership program at Duke University and plays a pivotal role in our risk modification project. She envisioned a truly innovative quality improvement approach that considers the role of *nature and nurture* by merging integrative medicine with our traditional oncology team in the overarching goal of care for the whole cancer patient.

Our oncology team, led by Charles Shelton, MD, focused on the conventional "nature" (familial and genetic) contributions to cancer risk in our breast cancer patients. Dr. Shelton heads our breast tumor board, which meets twice per month, where we discuss all new cases prospectively as a multidisciplinary team, including integrative medicine, and we test all patients for inheritable germline mutations based on recommended guidelines.[1] Though germline mutations are not modifiable in the conventional sense (you cannot change your family of origin), preventive strategies currently include prophylactic surgery (if deemed very high risk; e.g., BRCA mutation) and chemoprevention as potential interventions in very high-risk patients who are found to be carriers or who are otherwise very high risk (30+ percent lifetime risk of breast cancer). TOBH created a separate high-risk breast clinic based on this project and we follow all patients closely with pathogenic variants in their DNA and offer risk reduction based on National Comprehensive Cancer Network (NCCN) guidelines.[6]

The integrative medicine team focused on the complementary "nurture" (environment and lifestyle) component and how environmental modifications and lifestyle changes can help reduce recurrences in patients with cancer and even help to prevent cancer in non-cancer patients. Examples of these modifications include:

- Foods and supplements that diminish inflammation, including acetylsalicylic acid and nonsteroidal anti-inflammatory drugs
- Regular exercise
- A reduction in alcohol consumption
- Tobacco cessation
- Lower body fat and weight management
- Better sleep habits
- Stress reduction
- Access to spirituality and social support
- Similar whole-patient health approaches that promote stability in the genome.

If we could identify these risks clinically in patients already diagnosed with breast cancer, we believed that our team could identify and customize interventions relevant to our demographics to mitigate a patient's risks for future cancers. Further, we hypothesized that we could employ an appropriate model to change the lifestyle in the at-risk population by identifying women who would benefit most from risk-reduction strategies using available risk stratification such as the Gail model[7] or Tyrer-Cuzick tool.[8]

> From our pilot study, we identified an individual's modifiable and unmodifiable risks and developed customizable risk assessment tools appropriate for our general population based on these relevant data.

TOBH's cancer program began this holistic model of *nature + nurture* for breast care primarily as a pilot study in 2018 to examine collective risk factors for all of its patients with breast cancer living locally (i.e., not seasonal, vacationing patients). The model was then expanded in 2019 to include the at-risk unaffected population (without cancer) to better understand which factors might be modifiable in both patient groups. Stating this differently, the primary focus was therefore on developing a model program to help reduce cancer risk in patients with known breast cancer (e.g., current active patients). A secondary focus was the general population at risk that shares similar risk factors but in whom cancer has not been detected (e.g., screening population) where prevention was a long-term goal. This novel risk identification (using existing risk stratification tools) and customizable risk modification model, therefore, has a potential preventative application for both patient demographics: those with a personal history of breast cancer and those without it.

Our Study Methods

For the first part of our project, we performed an in-depth specific risk analysis of all patients with breast cancer treated at our small community critical access hospital population over three years (2016, 2017, and 2018). We later updated it with four-year data.[5] This analysis included a retrospective review of electronic health records (EHRs) for 165 patients, the majority of whom (>90 percent) Dr. Shelton evaluated and/or treated. Risk factors for breast cancer are well described in the literature. Therefore, we selected the majority of the known risk factors, tabulated these risks, and quantitated them within our known breast cancer population to see whether any results were outliers with respect to a reference population. To align data with our project goal, we separated the risks into two broad categories and tabulated each as "modifiable" and "not modifiable" (see Table 1, page 28). We queried the patient records for 46 risks, having identified 14 as "modifiable" risks and 32 as "not modifiable" risks. These were analyzed for each patient based on information in the patient's EHR. If information was lacking, it was scored as

Table 1. Risk Factors for Breast Cancer

Modifiable Risks	Not Modifiable
BMI	Gender
Exercise	Age
Diet	Ethnicity
Alcohol	T size (≤2cm, 2.1-5.0cm, >5.1cm)
Tobacco	Stage
Aspirin/nonsteroidal anti-inflammatory drugs	Receptors
Vitamin D	Family history first-degree breast cancer
Stress	Family history second-degree breast cancer
Sleep	Family history more than one first degree
Spiritual	Genetics
Support	Density on mammography
Night shift work	Menarche
Completed intended therapy	Parity
On aromatase inhibitor or tamoxifen if ER+	Age at birth of first child
	Breastfed
	Age at menopause
	Surgical oophorectomy
	Post-menopause hormone replacement therapy
	Oral contraceptive use
	Previous biopsy breast
	Personal history of breast cancer
	Previous ionizing radiation

unavailable. In earlier years, the patient EHRs had less information, particularly in the area of modifiable risks, which may skew the study results by presenting a lower number of modifiable risks. In other words, if providers had solicited more information, the average number of modifiable risks could potentially have been higher than our results show. Also of note, patients seen by oncologists often had better available information (e.g., family history, age of menarche, etc.) for all of these metrics than what was already in electronic records before a diagnosis of cancer was made, highlighting how the information available in mining data can vary greatly based on the historian (often primary care physicians [PCPs], who usually do not have time to complete full family history questionnaires).

It is possible to make an argument that several of the not modifiable risks identified in Table 1 are, in theory, modifiable. For example, if several decades ago a woman knew that she could lower her risk of breast cancer by planning the birth of her first-born child at an earlier age, she could have modified her risk. Similarly, a postmenopausal woman may choose not to take estrogen replacement therapy. However, for the purposes of the study analysis, we assumed—given that the median age of women in our study population was 63 years—that women were not then aware that having a first child at an older age was a risk factor for breast cancer, so we considered that metric unmodifiable. In our at-risk population (younger age, no cancer), these could, of course, be considered modifiable through timely education.

As hypothesized, our analysis of patient records revealed many cumulative risk factors for breast cancer, because the analyzed population already had breast cancer. Though we acknowledge that this biases the study results, we were unable to simultaneously perform a control arm study of the normal non-cancer population to see whether rural risk is inherently high due to Health Insurance Portability and Accountability Act concerns in accessing women's records without informed consent. We are currently performing a parallel study on the patient population without cancer as part of an institutional review board-approved study based on these same pilot data. Preliminary results from that study confirm the same findings of higher-than-expected familial clustering and other associated high risks in the at-risk rural population as well (e.g., high BMI and high alcohol use, poor diet and exercise, and high familial risks). In the unaffected population, for example, familial cancer is also high: 41 percent of women screened report strong family histories of breast cancer; 8 percent have ovarian cancer; and 5.3 percent have pancreatic cancer in their families. Overall, 21 percent of all screened patients without breast cancer at the time of mammography meet NCCN guidelines for genetic testing for hereditary breast and ovarian and pancreatic cancer.[9] This means that one in five patients in our screened population should be considered for genetic testing for hereditary breast and ovarian and pancreatic cancer. Additionally, in high-risk patients identified by our current risk assessment tool (Tyrer-Cuzick), most women share the same modifiable risks of higher-than-normal body weight, poor diet, and inconsistent exercise, and they could benefit from this approach of modifying their risks through lifestyle changes as well.

From our pilot study, we identified an individual's modifiable and unmodifiable risks and developed customizable risk assessment tools appropriate for our general population based on these relevant data. Though it may seem strange at first to examine the collective risk factors in a patient who has cancer, we were using our findings to identify risks that are modifiable versus those that are not and then offer customized interventions. Again, we acknowledge that some of the known risks cannot be changed (gender, age, menopause age, age of menarche, height, ethnics, family history), but our hope was to identify those that are modifiable, study them in the context of a model providing holistic interventions through integrative medicine approaches, and extend our model to other programs seeking to lower the future risks of secondary cancers and/or proactively prevent primary cancers. Accordingly, we have now integrated the same model into our risk reduction model for unaffected women as a primary form of cancer prevention.

Results from Our Breast Cancer Risk Analysis Quality Study

We discovered several interesting outcomes from this quality study: First, we found that most patients with breast cancer had many known collective high risks for breast cancer, many of which are modifiable given appropriate education and patient motivation. The median number of modifiable risks per patient was 4, with a range of 0 to 14. The median number of not modifiable risks was 10, with a range of 0 to 32. The typical person with breast cancer in our study collectively had 14 of 46 total potential screened risks, one-third of which are modifiable.

Second, we found that the most prevalent and significant risk factors in our population rurally were a positive family history of breast cancer (or ovarian cancer) in more than 55 percent and an elevated BMI in 70 percent. High breast density was also remarkably common on imaging (40 to 50 percent had heterogeneously or very dense breasts on imaging, both of which can increase the risk of breast cancer by a factor of 2 or more compared to fatty breasts).[10] These are clearly not all modifiable risks, but they can be modeled and used for targeted interventions. Because we have many families with first-degree and second-degree relatives affected by similar cancers and disproportionately high percentages of people with high BMI, we chose the Tyrer-Cuzick tool, which accounts for these risks and, in the recent 2019 version of the tool, for breast density. Accordingly, based on our demographics, our team adopted the Tyrer-Cuzick model v8[11] to stratify these risks and better identify at-risk women for referral to a high-risk breast clinic, which was our initial vision with this plan. We implemented our high-risk breast clinic in July 2019 in our screening (unaffected) population as a direct result of this breast cancer risk analysis study, and we now refer all patients with an absolute lifetime breast cancer risk of 20 percent or higher to that specific clinic and simultaneously to the risk modification program as appropriate. To date, using this model in 4,500 women screened annually in our rural population, 7.5 percent of unaffected women (N = 337 estimated by July 2020) have lifetime breast cancer risks greater than 20 percent. We offer each woman participation in this program, as well as following them in a high-risk breast clinic, which includes additional imaging, risk modification through our integrative medicine team, chemoprevention when indicated, and genetic testing when appropriate. See Figure 1, page 30.

Third, we discovered that the majority of patients had several modifiable risks where intervention was indeed possible. Most commonly, these were elevated BMI (weight), poor diet, excess alcohol consumption, poor exercise habits, and smoking. The median number of modifiable risks (per patient) in our population of breast cancer patients was 4/14; several patients had 8/14 modifiable risks (the maximum identified in any study patient). No patient had every risk (14/14). These data suggested a potential to greatly impact our patient population's risk for second breast cancer or risk for recurrence through holistic interventions and perhaps extending this model to individuals in the at-risk population who do not currently have cancer but who likely share the same biological and environmental risks. Only 3/165 patients in our analysis had no identifiable modifiable risks, but that could be explained easily by poor documentation early on in our records. Stated another way: Analyzing three years of data from our resident population of patients with breast cancer, we found that 98 percent had some modifiable risks where intervention could be potentially effective in future cancer prevention. Figure 2, page 30, lists the top five modifiable risks.

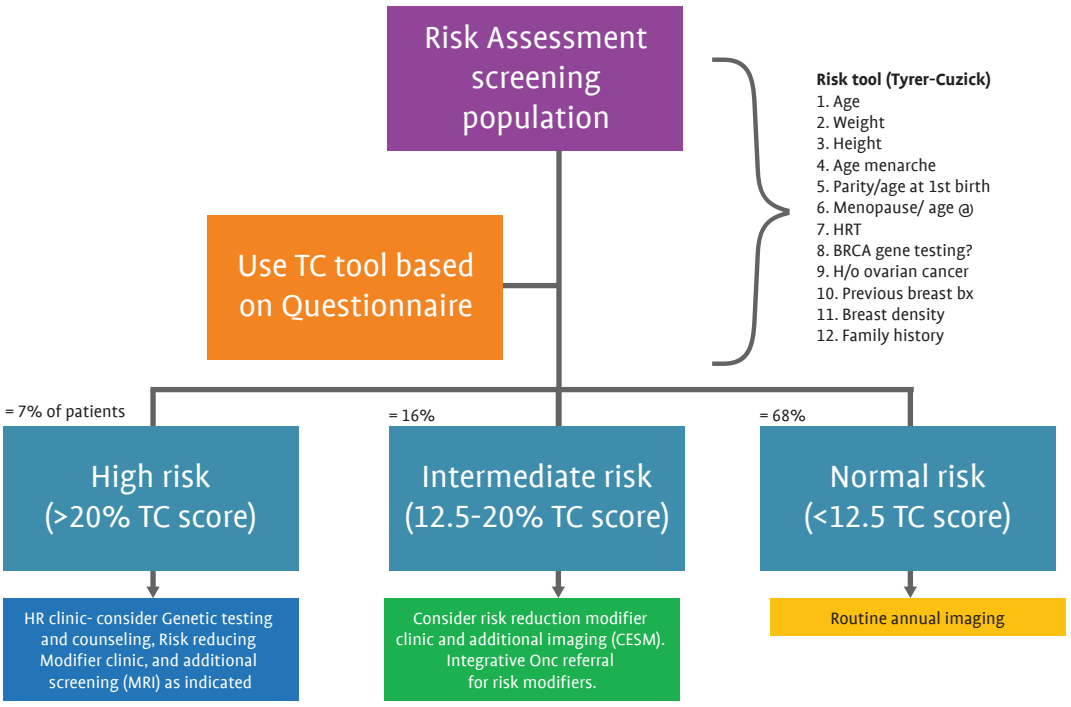
The Role of Integrative Medicine

The literature has shown that adding an integrative medicine program to a traditional oncology program can improve the care of oncology patients. As such, ASCO (the Association of Clinical Oncology), the Society of Integrative Oncology, and the National Cancer Institute now include integrative oncology as category 1 and 2 evidence-based approaches to integrative cancer care.[12,13] We found that our patient population has embraced the model in which we combine conventional care and complementary therapies. It is the perfect blend of nature and nurture.

As a small community cancer program, we are fortunate to have a physician who is board certified in integrative medicine, and since early 2017 we have added this clinician prospectively to all case discussions at every tumor board. Now, three years later, we continue to use and expand on these services. In 2018, the authors of this article presented TOBH's use of integrative medicine at the meeting of the Society of Integrative Oncology as a best practice model on how integrative techniques can complement and enhance patient care.[14] Our team believes that every patient benefits from integrative medicine. When modifiable lifestyle risk factors for cancer occurrence or recurrence are a focus, the benefit of integrative medicine becomes even more evident.

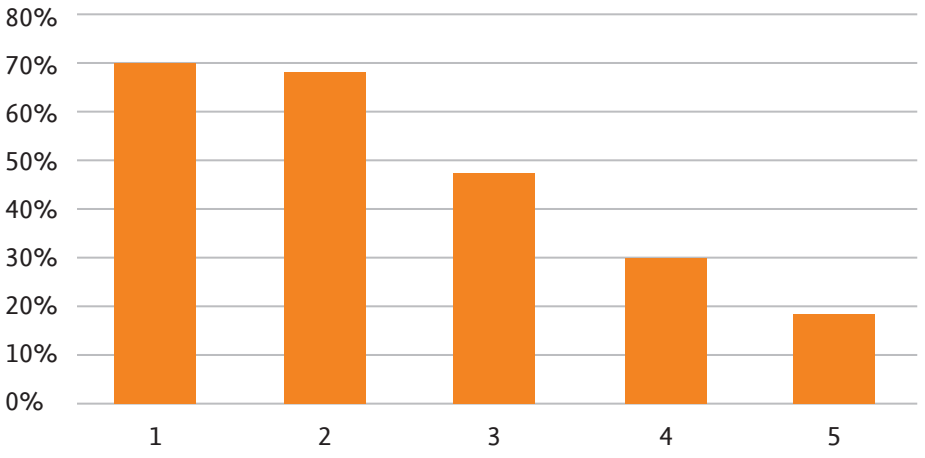
An integrative medicine physician has not only helped us manage patients during active therapy by mitigating nausea and neuropathy and other chemotherapy, hormone therapy, and radiation treatment-related side effects through various complementary approaches but has also enhanced the overall care of our patients. With a holistic focus, the integrative care continuum

Figure 1. The Outer Banks Hospital Risk Assessment Model*



*This model is used to assess risk in the general population for breast cancer given high familial clustering in first- and second-degree relatives, high BMI rates, and high breast density, as well as other risks we examined. We have found the Tyrer-Cuzick model best suited for these metrics. CESM = contrast enhanced screening mammogram.

Figure 2. Top 5 Modifiable Risks by Rank



Poor diet (#1) in 70% of all patients

Elevated BMI (#2) in 68% of all patients

A sedentary lifestyle (#3) in 48% of all patients

Alcohol use (>1 per day) (#4) in 31% of all patients

Current tobacco (#5) in 18% of all patients

n = 161

can encompass a discussion of life stressors, social and family support, spirituality, mindfulness and stress adaptation/reduction techniques, diet quality and supplements, exercise specifics and frequency, sleep patterns, tools to achieve healthy outcomes, and more.

As we move into the next phase of our risk modification model, which focuses on how best to customize and integrate interventions targeted to modifiable lifestyle factors into long-term care, our patients with breast cancer will benefit from integrative oncology care as part of their overall survivorship care.

With the quantitative risk factor analysis of our patients with breast cancer completed in 2018, we hypothesized that our patients with breast cancer could benefit from several risk modification strategies led by the integrative medicine physician as part of our Integrative Oncology Program. Our integrative medicine physician customizes interventions throughout a patient's entire course of therapy, including lifestyle, eating habits and alcohol consumption, sleep, and stress reduction. Because a large portion of our integrative program is focused on mindfulness, stress reduction, and quality of life, we engaged our breast care team to discuss risk modifiers with their patients with breast cancer and help patients set their own goals for change. With the addition of these integrative services, our breast care program has evolved into truly customized precision care.

Using evidence-based literature, we share the relative risks (hazard ratios and each risk factor's potential impact on their outcomes) of each modifiable factor with our patients, empowering patients with information so that they can make their own modification goals. Although lifestyle recommendations from the American Cancer Society[15] and ASCO[16] include similar risk reduction guidance, we have found that patients are not aware of how—when taken together—taking proactive steps can help reduce their risk of second cancers. We give them data to show them how much it can add to their outcomes as it becomes part of a proactive survivorship plan.

It is our opinion that integrative medicine and traditional oncology care as a blended model can synergistically lower the chances of recurrence of cancer in existing patients with cancer as much as traditional therapies, such as anti-estrogens in ER+ breast cancer, which is our most common occurrence. Most people are simply not aware of integrative medicine options. Our physician champion is ideal for offering this education, and our Cancer Committee fully embraces this model. Additionally, we believe that most traditionally trained physicians are reluctant to attempt lifestyle modifications in their patients, because they can be truly hard to change, but TOBH has embraced integrative medicine as a critical component of our cancer services. Moreover, we are not alone in our efforts. Others in the academic cancer community also consider these metrics important; for example, the recent Breast Cancer Weight Loss Study randomized study, which is looking at body weight reduction, along with exercise, will have data forthcoming in the next few years.[17]

Early data from randomized trials now show that active exercise lowers the risk of recurrence of cancers in comparison to sedentary lifestyles. Similarly, other modifiers, which we also believe act as epigenetic modifiers, can reduce the risk of recurrence of the same cancer or a possible second cancer, particularly in breast cancer, where the majority of second cancers occur many years and/or decades later and are often estrogen mediated. Many of our modifiable factors lower estrogen; for example, weight loss, BMI reduction, alcohol minimization, and improved diet. Our study revealed even more concentration of these modifiable risks in those women with second cancers (on average 20 years later), with 90 percent of second cancers in our women occurring in those with BMI > 25, suggesting that lifestyle and obesity greatly contributed and therefore these women could potentially benefit even more from adopting changes for these modifiable risks. Because these are clearly risks that we can change though programmatic efforts, TOBH has incorporated this information into this wellness approach to all patients with breast cancer.

Educating Our Providers and Patients

Despite mounting evidence that lifestyle choices (tobacco cessation, exercise, healthy diet, stress reduction) play a role in helping to prevent cancer, often these components of whole-patient wellness are not emphasized or even discussed by oncologists. Further, a 2008 study showed that patient adherence is poor, with only 5 percent of cancer survivors meeting all of a set of three basic recommendations (diet, physical activity, and smoking cessation), and taken alone, compliance in each area was poor.[18]

Very few physicians or providers take the time (or have the time) to explain to patients what their risks are and how they can reduce them. In our limited experience, all patients are interested in this information, but it is hard to find anyone willing to sit down with patients to help share its relevance. A study of childhood cancer survivors support this, where less than one-fifth of patients (18 percent) had visits with their providers in follow-up to discuss risks of future cancer and ways to screen for or reduce the risks of second cancers and other poor outcomes.[19]

Prior to the addition of our integrative medicine program, TOBH did a poor job of sharing this information and educating its patients, which may have influenced the recurrence rates noted in our quality study. In that analysis, second cancers in patients with previous breast cancers accounted for 15 percent of our total breast cancer cases. Among those patients, the analysis showed an even higher concentration of elevated BMI (90 percent of patients with second cancers had high BMI and were post-menopausal) and familial histories of cancer (100 percent of second cancer patients had a family history of breast cancer in addition to their own previous breast cancer). Our study revealed that prior to 2018, very few EHRs showed any discussions about lifestyle considerations or any mention of modifiable risks other than what we included in survivorship plans, which was very generic. With the addition of an integrative medicine physician to our team, this became a focus for our cancer program and is now part of ongoing active survivorship. Patients are seen at intervals during and after therapy regularly as part of routine care. In addition, in 2018, to help improve patient education about these risk factors, we shared data on the various risk factors and their relative effects on cancer occurrence and potential

Dr. Christina Bowen consulting with a local cancer survivor.

recurrence with our oncologists and our PCPs (see Table 2, page 33).

To show the potential benefits of modifying these risk factors, we proactively engaged our local breast cancer patient population, discussing their individual risks and explaining how these may potentially correlate with recurrence and/or new cancers. Since 2018, all patients with breast cancer now see our integrative medicine physician for an initial risk-reduction consultation. Patients learn which modifiable risk factors apply to them and the potential benefits from taking action to modify these customized risks. We provide patients with evidence-based information and review the anticipated benefits of various risk reduction strategies, including the estimated relative benefits of each, and let them choose, for example:

- Exercising regularly can lower risk of breast cancer by up to 20 percent
- Weight loss/BMI reduction can reduce risk by 10 percent per 5 BMI points
- Improved diet can reduce risk by 11 to 15 percent
- Moderating alcohol can reduce risk by 67 percent
- Quitting tobacco can reduce risk by 15 percent
- Supplementing with vitamin D if patients are deficient (or maintaining normal levels) can also reduce risk.

We highlight the risk factors that patients can control and modify and the ones they cannot. This is similar to a model in childhood cancers that highlights the relevant idea that the risk and severity of outcomes (vis-à-vis complications, or second cancers) are potentially modifiable by preventive strategies that encourage healthy lifestyle behaviors, specialized surveillance and screening, and risk management.[18]

We share these data proactively with our patients by introducing the idea early in their cancer journey and then again throughout their various treatments. We reinforced the idea at multiple touch points with various providers. Near the end of their primary therapy (typically, radiation therapy is last), we then encourage patients to choose their own personal goals from among these modifiable risks. Once the patient's goals are identified, we provide resources to meet these objectives through our Wellness Center, which includes our integrative medicine physician, a nutritionist, and a health coach, among others. Patients define their own goals based on their unique situations, finalize these goals in our "modifiable risk" clinic, and are then held accountable on all subsequent follow-up visits as goals are shared with their primary care providers as well as all oncology team members. Patients are supported both by their PCP and by the oncology team to improve their overall health in ways that we know will improve not only disease-specific survival but also overall survival due to the potential to affect other chronic diseases. Metrics are tracked and reviewed with patients at follow-up visits with support provided by our integrative oncology team. Because the median number of modifiable risks is four in most patients, we ask that patients usually work on three to four goals in their first year. Each goal is customized to their unique needs.

We believe that this risk modification model serves as a great liaison between our chronic disease team and our oncology providers and promotes not only self-empowerment but also better communication between PCPs and oncologists. These goals (often BMI reduction, minimizing alcohol intake, exercising more) often benefit patients in other ways, so our PCPs embrace the risk modification model. We believe that this innovative approach results in better care coordination and broader patient engagement. Furthermore, we have found that 98 percent of our patients have at least one modifiable risk that they are willing to try to improve. Several patient case studies follow.

(continued on page 34)

Table 2. Risk Factors and Relative Risk of Cancer Occurrence and Recurrence

Factor	Relative Risk
	Very High/Effect
Ionizing radiation <30 years of age	22-40×
Personal history of LC15	8-10×
BRCA1/BRCA2 mutations	3-7×
Other genetics: TP53, ATM, CDH1	4.0-8.0×
CHEK2, PTEN mutations	2.1-4×
<50-year-old woman with first DR breast cancer (1-3)	2.0-12.0×
≥50-year-old woman with first DR breast cancer (1-3)	1.6-2.6×
Age (70-74 vs. 30-34)	18×
Age >65	4×
Age at first birth (>30 vs. <20)	1.9-3.5×
Bone density (highest quartile vs. lowest)	2.7-3.5×
Breast density on mammography (dense vs. fatty)	1.8-6.0×
History previous breast biopsy benign	1.7×
History ADH on biopsy	3.7×
Personal history of breast cancer <40	>2×
Ashkenazi heritage	3-5×
	Moderate Risk/Effect
Alcohol use	1-2×
Early menarche (<12-13)	1-2×
Height	1-2×
BMI > 25	1.25-1.32×
High socioeconomic status	1.1-2×
Oral contraceptive use (past use/current vs. never)	1.07-1.2×
Post-menopause hormone replacement therapy (current vs. never)	1.2x
Dense breast (25%-50% vs. fatty)	1.1-2×
Personal history of breast cancer before age 40	1.1-2×
Late menopause (>55)	1.1-2×
Diabetes mellitus type II	1.1-2×
Tobacco use	1.1×
Night shift work	
Not completed intended treatment	?
Breastfed (>16 weeks vs. less/none)	0.73×
Party (>5 vs. none)	0.71×
Recreational exercise	0.70×
Post-menopause BMI <25	0.63×
Oophorectomy by 30 years old	0.30×
Aspirin/nonsteroidal anti-inflammatory drugs	0.79×

Notes: DH = degree relative; ADH = Atypical Ductal Hyperplasia.

(continued from page 32)

Case Study One

A 65-year-old post-menopausal female with stage IA ductal carcinoma with estrogen and progesterone receptor positive (ER+ PR+) markers and a history of elevated BMI at baseline with plans to start aromatase inhibitors or tamoxifen was offered weight reduction and/or weight stability via exercise and diet as way to further minimize the risk of breast cancer recurrence. She was encouraged to pick three metrics (weight loss to help BMI, diet changes, regular exercise five days a week) among others unique to her risks as potentially modifiable goals at the time of her risk reduction consult, which is typically at one month following the last treatment. Over the first year, we followed up on these measures at subsequent visits, usually at three months, six months, and annually. Because most of our patients (87 percent) have hormone receptor-positive breast cancers, where these risk factors more tightly correlate with cancer-specific recurrence, we think that this program will magnify favorable outcomes.

Case Study Two

A 42-year-old female with breast cancer at presentation had a borderline high BMI (26), a poor diet, and inconsistent exercise regimens; she also wanted to reduce her stress during and after her treatments. She drank more than seven glasses of wine a week and embraced a model in which these risks could be explained to help her modify her lifestyle. She was found to be BRCA positive, as well, and had further risk reduction surgeries, including oophorectomy and bilateral nipple-sparing mastectomies. Though her risk reduction is less likely to be mitigated by her lifestyle than by her surgeries, her recurrence rates and her overall health clearly benefit from the changes we implemented. Her weight is ideal now (BMI < 25), her alcohol consumption is three glasses per week, and her exercise is regular now. She remains recurrence free.

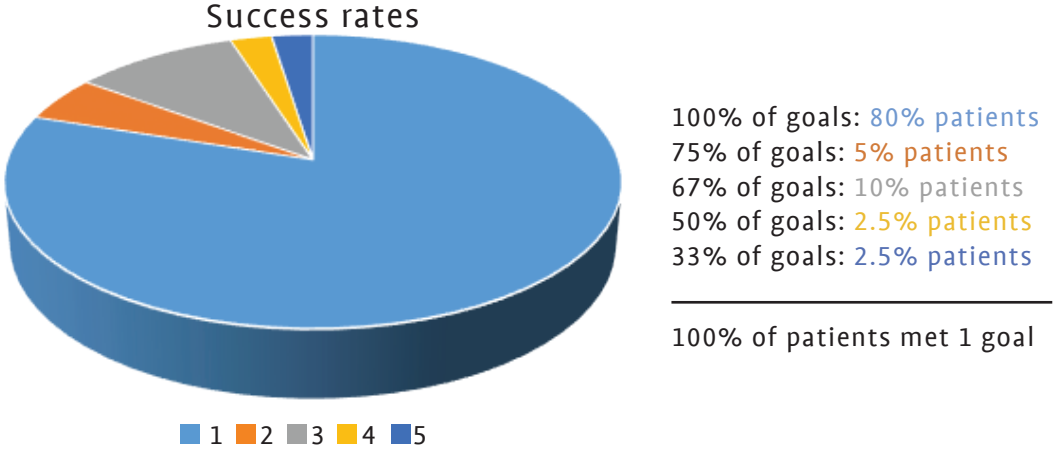
Case Study Three

A 53-year-old female with ER+ breast cancer has a strong family history of breast cancer but negative genetics and had a high BMI at baseline and is a smoker. She chose weight reduction, especially knowing that she may gain weight on aromatase inhibitors, taking weekly yoga and Pilates classes. This patient also chose smoking cessation as her second custom risk modifier. We connected the patient to a smoking cessation clinic that we offer and followed up with the patient at our Wellness Center. She achieved all of her goals.

Looking Ahead

Since starting this risk modification model, TOBH has found that its patients are enthusiastic and willing to embrace the factors they can control themselves. We have strong buy-in from our oncologists, who now consistently refer patients to our Wellness Center, headed by Dr. Bowen. To date every patient referred for this model of risk modification has bought in to the program, and we are tracking data as a part of a follow-up QI project. Thus far, 64 patients with breast cancer have been enrolled in this integrative model and 100 percent have achieved at least one goal of risk modification (e.g., improved diet), and 80 percent of patients have achieved every goal (most commonly increased exercise, weight management, and improved diet). See Figure 3, below. Contrast this success to the 5 percent results cited earlier in a 2008 study.[18] It is interesting to anecdotally note that when patients are empowered to make their own goals and choices rather than providers telling them what they "should" do, there is considerably more success. We have also found that this model excites PCPs because these cancer-specific goals are mostly free of cost, and the same lifestyle goals often help with other chronic diseases (e.g., hypertension, type II diabetes, hyperlipidemia, coronary artery disease, vascular disease, etc.).

Figure 3. Results—Early* Success



* Average f/u is 10 months, range 4-28

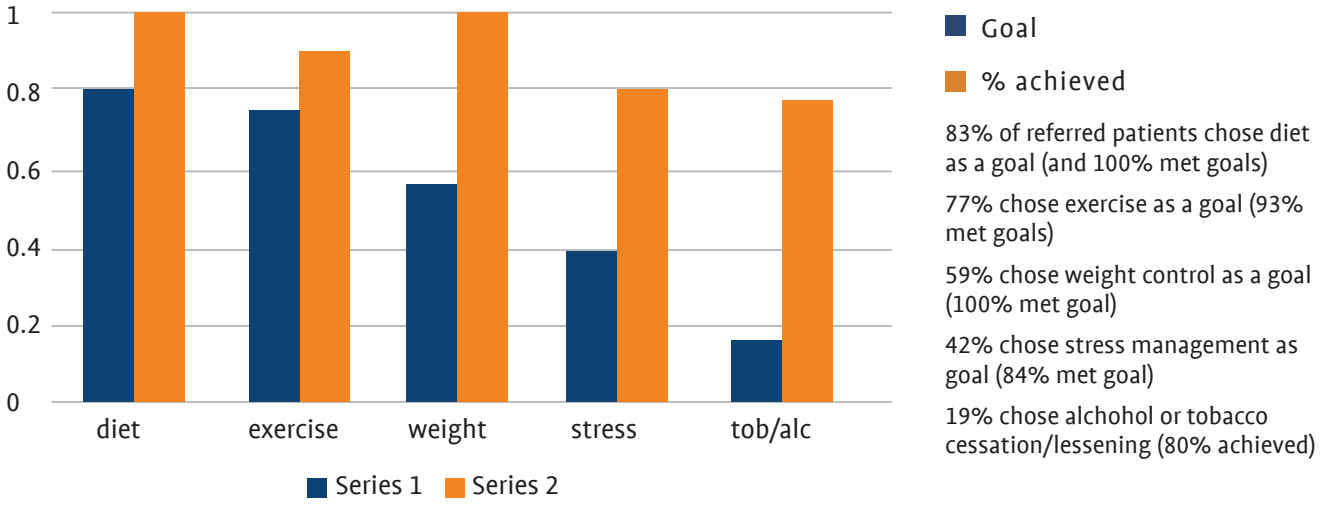
One other surprising outcome from this QI project was the amount of non-compliance we found in women with breast cancer in regards to hormone therapy; 13 percent of patients with ER-positive breast cancer were discovered to be not compliant with hormone therapy (anti-estrogen therapy in ER-positive cancers) in this study due to side effects most often (and therefore discontinued use) and a general lack of an understanding of the continued need for maintenance. This rate of 87 percent compliance is below the CoC reference standard of 90 percent,[20] which is a national target in quality programs, again highlighting how disparity can easily creep into rural areas. Most women, and even some PCPs we found, did not realize that it lowers the relative risk of recurrence by 50 percent, and many PCPs assume that oncologists are following all of these patients when in fact rurally they may not be. We have since added this metric to our risk modifier checklist (even making it a goal to minimize side effects from hormone therapy) and now rely on our integrative medicine team as a tool to help mitigate the negative effects of hormone therapy (especially weight gain and vasomotor symptoms) and thereby increase compliance rates with hormone therapy for breast cancer patients. Anti-estrogen therapy is pharmacologically the greatest modifier of recurrence/occurrence, and we have already seen an improvement in compliance with hormone therapy in our patient population accordingly (we are consistently >90 percent). If no other measures of success emanate from this risk modification program, our process has already succeeded in improving these statistics by this measure alone.

To date, we have referred all interested newly diagnosed patients with breast cancer who have at least one modifiable risk (98 percent of our analyzed patients) who we believe can benefit from this process of education and personalized goal setting and then measured accountability by the oncology team. Figure 4, below, shows the outcomes from this approach since we started. The majority of patients referred to our Wellness Center hit every metric and maintained their goals over time. The average weight loss in patients choosing that specific goal was 13 pounds, and 100 percent of patients with weight management as a main goal achieved their goal. We have also seen our second cancer rates decline in these patients, but this metric will need 10 to 15 years of follow-up to be considered real.

By innovatively empowering our patients to become their own risk-modifying tool, we engage more patients and potentially lower the risk of recurrence of future cancers. Furthermore, an added benefit to their health from these improved self-selected lifestyle choices is that they help in chronic disease management (e.g., diabetes, cardiac disease, etc.). By engaging patients, setting goals with them, showing them the potential magnitude of those changes, and then holding them accountable to themselves and to us, we are improving overall health and quality of life of our breast cancer patients. We plan a follow-up analysis of these benefits in future projects.

Plans include expanding this holistic model to other cancer sites with similarly modifiable risk factors and into other at-risk populations before cancer is even diagnosed. For example, as stated earlier, by analyzing these data we discovered that based on familial history, dense breasts, and high BMI, we have a high-risk population in which mathematical modeling helps to stratify risk for better targeted screening in breast care. For this reason, we now use the Tyrer-Cuzick model (v8)[11] to calculate lifetime risks for breast cancer in our screening population in order to appropriately offer genetic testing to identify unmodifiable risks (family history and heritage), as well as to assign patients to low-, intermediate-, and high-risk groups for various risk reduction strategies and alternative secondary screening. Since implementing

Figure 4. Success by Goal



this strategy, based on NCCN guidelines, we have discovered that 7.5 percent of our population at any given time are high risk, defined as lifetime risk of breast cancer greater than 20 percent, 16 percent are at moderate risk (defined as 12.5 to 20 percent), and 76.5 percent are low risk (defined as <12.5 percent lifetime risk of breast cancer). From the perspective of risk modeling, 23.5 percent of our patients carry the majority of high and moderately high risks collectively. We currently contact all high-risk patients we have screened and see them in consultation to discuss this model and enroll them into our high-risk (unaffected) breast clinic. Our plan is to expand this model to include both the high- and moderate-risk groups that could each benefit the most from this approach of risk reduction via our integrative medicine team (see Figure 1, page 30). Plans include duplicating this model for other cancer types where we identify modifiable risks.

Our integrative medicine and wellness team is a valuable part of this risk model by offering lifestyle choices, which we believe can be as preventative as other modalities, and it is affordable and certainly less invasive. By offering risk reduction through education about BMI, exercise, diet, stress reduction, alcohol moderation, and smoking cessation, among others, we feel that we can lower the chances of developing cancer as much via alternative and complementary approaches as we can through traditional medicines. In other words, we believe that the effects of these modifiers can be as powerful in relative risk reduction, especially if patients are empowered with this information.

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