



# Do Women With Breast Cancer Who Choose Adjunctive Integrative Oncology Care Receive Different Standard Oncologic Treatment?

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Leanna J. Standish, ND, PhD, LAc, FABNO<sup>1</sup>, Fred Dowd, BA<sup>1</sup>,  
Erin Sweet, ND, MPH, FABNO<sup>1</sup> , Linda Dale, CCRP<sup>1</sup>,  
and M. Robyn Andersen, PhD, MPH<sup>2</sup> 

## Abstract

**Purpose:** To determine if women with breast cancer who choose adjunctive naturopathic oncology (NO) specialty care receive different standard oncologic treatment when compared with breast cancer patients who receive only standard care. **Participants:** Women with breast cancer stages 0 to 4, aged 18+ who spoke English and sought care from outpatient naturopathic doctor clinics were enrolled in an observational study of clinical and quality of life outcomes. Women who sought NO care 2 or more times within the first 2 years postdiagnosis were identified as NO cases. A matched comparison group of breast cancer patients were identified using the Western Washington Cancer Surveillance System (CSS). **Methods:** A longitudinal cohort design. In addition to self-report data, the CSS provided data on demographics, stage at the time of diagnosis, and initial treatment. Oncology medical records were abstracted in order to provide additional information on standard oncologic treatment for all participants. **Results:** Cohorts were well matched with regard to demographic, histologic, and prognostic indicators at the time of diagnosis. Approximately 70% of women in both cohorts received standard oncologic care that met the National Comprehensive Cancer Network guidelines. There were no statistically significant differences between the cohorts in treatment received. Fewer women in the NO cohort with estrogen receptor–positive breast cancer appear to have received antiestrogen therapy. **Conclusions:** Women in both cohorts appear to receive guideline-concordant care. However, women who receive adjunctive NO care may be less likely to receive antiestrogen therapy.

## Keywords

complementary and alternative medicine, breast cancer, integrative oncology, observational study

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## Introduction

Women with breast cancer in the United States increasingly use complementary and alternative medicine (CAM) as part of their treatment. As more data emerge linking diet, lifestyle, and immune status to cancer risk and survival,<sup>1–5</sup> breast cancer patients seek out professional advice regarding nutrition, exercise, herbal and other supplements, and mind-body medicine.

Naturopathic physicians with specialty training in oncology offer a diversity of evidence-based CAM practices to assist patients with cancer during their treatment and recovery. Adjuvant naturopathic oncology (NO) includes natural medicine procedures (acupuncture, hyperthermia), nutritional and lifestyle counseling, as well as botanical and

nutritional medicines (supplements). For the purposes of this study, we defined NO as medicine practiced by naturopathic doctors (NDs) who are board certified in NO (Fellows of the American Board of Naturopathic Oncology [FABNO]), some of whom are also licensed acupuncturists in Washington State, where NDs are licensed to practice medicine. ND office visits and procedures are reimbursed by medical

<sup>1</sup>Bastyr University Research Institute, Kenmore, WA, USA

<sup>2</sup>Fred Hutchinson Cancer Research Center, Seattle, WA, USA

### Corresponding Author:

Leanna J. Standish, Bastyr University Research Institute, 14500 Juanita Dr NE, Kenmore, WA 98028, USA.

Email: ljs@bastyr.edu



insurance companies in some states in the United States, including Washington State.

In order to understand the effect NO has on treatment outcomes for women with breast cancer, we need to understand not only the care they receive from NO providers but also if NO care users fail to receive important elements of conventional care. Other reports have described poor outcomes for women who forgo conventional care.<sup>6,7</sup> There is also evidence that NO care users may differ in their use of conventional care such that while CAM users are more likely generally to get mammography, women who see only CAM providers for primary care are less likely to receive screening mammography.<sup>8</sup>

While we have previously reported that women who seek NO care do not appear to delay initiation of standard breast cancer treatment, with this report, we characterize the cohorts and examine the type of conventional therapies NO patients receive examining the hypothesis that their treatment differs from that received by women who receive only usual care.<sup>9</sup> More specifically, we sought to answer the following questions: Do NO patients differ from usual care patients in the histologic subtypes of their cancers? That is to say do women who seek NO care have potentially more difficult-to-treat cancers such that matching by stage would fail to provide groups of similar prognosis? With regard to treatment we asked: Do NO patients receive different types of surgery or differ in the extent of their surgical treatment? What percent of NO patients receive National Comprehensive Cancer Network (NCCN) guideline-concordant care? Are women who seek NO care more or less likely to have received recommended treatments?

## Methods

This observational study was designed to describe and explore differences in the health-related quality of life, clinical outcomes, and conventional treatment differences between women who receive NO care and a matched comparison usual care cohort. This report describes those results through their first year of treatment.

This longitudinal assessment evaluated women who received NO treatment from 6 outpatient ND clinics located in Western Washington State ( $n = 193$ ) and a larger matched comparison group ( $n = 360$ ) women identified and recruited from the Western Washington Cancer Surveillance System (CSS) between February 2, 2009, and April 14, 2014. Cases and comparisons were matched based on demographic characteristics and Surveillance, Epidemiology, and End Results (SEER) summary stage of cancer as recorded by CSS at time of diagnosis. Women were eligible for the study if they spoke English fluently enough to complete surveys, were more than the age of 18, and were diagnosed with breast cancer less than 2

years prior to their first ND clinic visit. Comparison women were identified in CSS based on their similarity to an enrolled NO cohort patient. Study methods and questionnaires were approved by the institutional review boards of the Fred Hutchinson Cancer Research Center in Seattle, Washington, and Bastyr University in Kenmore, Washington.

### *Enrollment of NO Cohort*

In Washington State, NDs are licensed as physicians and enjoy mandatory insurance coverage under the Every Category of Provider law passed in 1996. NO treatments for cancer may be covered by some insurance plans. All NO care was provided by NDs with board certification in NO. Patients at the NO clinics received conventional oncology treatment from a variety of local providers and Western Washington regional cancer centers. Although patients were recruited from a total of 6 NO clinics, most (74%) in this sample were treated at a single clinic. At this primary clinic, most women were approached at their first clinic visit. Potential participants received a packet containing the informed consent form, a medical records release form, and an enrollment questionnaire. In most cases, informed consent was obtained during the appointment, and all study documents were completed prior to leaving the office. In a few cases, women took the packet home to review and complete the forms. Women recruited from the other participating NO clinical sites were given or sent the same study packet at a clinic visit within 3 months of their first clinic visit. In these cases, informed consent was administered by phone.

### *Identification of Potential Matched Comparison Usual Care Patients*

Women enrolled in the NO cohort were identified in CSS in order to collect data on their diagnosis and treatment for matching purposes. CSS was then queried to identify breast cancer patients who matched the enrolled NO cohort women by stage at diagnosis and demographic characteristics including age, ethnicity, and marital status.

### *Enrollment of Matched Comparison Usual Care Patients*

Women identified through CSS received a letter from CSS explaining the purpose of the registry and determined their interest in research participation. Three weeks following the initial letter, a research packet containing a cover letter, a baseline questionnaire, 2 copies of the informed consent, 2 copies of the medical records release form, and a stamped return envelope was sent to women who did not decline research participation.

Approximately 3 weeks after the packet was sent, women who did not respond received a call from study staff. Of 877 women approached to participate, 4 had passed away between the time they were identified in CSS and the initial mailing, 66 (5%) could not be reached at the address recorded with the registry, and 360 (38% of those approached) returned the forms including the completed questionnaire.

### Measures and Data Collection Sources

**Overview.** Information on age, demographics, marital status, stage of cancer, histology, standard treatments received, date of diagnosis, and ethnicity of all enrolled women were provided to the study by CSS. These data were used to develop an assessment of receipt of NCCN guideline-concordant care. Additional information on participants' cancer at diagnosis and treatment received was collected via chart abstraction of medical records. A more detailed description of these methods may be found in our earlier articles.<sup>10,11</sup>

### Questionnaire Data Collection Methods

Questionnaires were completed by patients as part of study enrollment. Data from questionnaires were checked for missing and unusual or impossible responses as they were data-entered. Quality assurance (QA) efforts included double data entry with computer-assisted and manual review of questionnaires for discrepancies. QA checks were performed on 100% of all baseline questionnaires. QA checks using the same procedures were also conducted on 10% of all other questionnaires, including 6- and 12-month follow-ups. Discrepancy-checking questionnaires revealed an accuracy rate of greater than 98% for questionnaires in any batch and category.

**Cancer Registry Data.** CSS is part of the SEER program of the National Cancer Institute. The CSS was established in 1974 under contract with National Cancer Institute's SEER program. Its mission is to provide high-quality data on the incidence, treatment, and follow-up on all newly diagnosed cancers (except non-melanoma skin cancers) occurring in residents of 13 counties in northwest Washington State. As of 1992, cancer diagnoses were required by state law (R.C.W. 70.54.230, 70.54.250, 70.54.260, 70.54.270) to be reported to the Washington State Department of Health for the purposes of understanding, controlling, and reducing the occurrence of cancer in Washington State. Data on cancer cases are obtained by the CSS through hospitals, outpatient surgical centers, pathology laboratories, radiotherapy centers, selected clinician offices, and through review of death certificates. Confidential CSS data are only made available to qualified researchers whose projects have been reviewed

and approved by a Health and Human Services registered institutional review board.

CSS provided data on the demographic (age, race, ethnicity, and marital status), disease characteristics (stage at diagnosis, date of diagnosis), and initial treatment (dates and kinds of surgeries, use of radiation therapy, dates and kinds of chemotherapy prescribed) for women in both cohorts.

**NCCN Guideline-Consistent Care.** Data from CSS were used to develop a measure of NCCN guideline-consistent care. We used methods developed by Hassett et al to evaluate both the appropriate use of recommended treatments and the inappropriate use of unnecessary treatments for breast cancer based on consensus- and evidence-based clinical practice guidelines.<sup>12</sup> Twenty-seven surgical, radiation, and chemotherapy quality measures based on recommendations made by the NCCN were evaluated. Because the measures evaluated different aspects of care, patients could be assessed on more than one measure. Twenty of the measures assessed underuse of recommended treatments (such as failing to provide radiation therapy when it would be recommended), and the other 7 examined overuse of treatments (such as use of chemotherapy when not recommended). Each participant's treatment was then evaluated as meeting, not meeting, or exceeding the NCCN guidelines for standard breast cancer treatment based on compliance with the guidelines assessing underuse and overuse. These measures were then used to describe the percentage of patients in each cohort who received treatment consistent with all 27 guidelines, and separately with the 20 based on underuse measures and the 7 unnecessary therapy measures.

### Medical Records Abstraction Methods

Data on conventional treatments received beyond those recorded by CSS were collected from conventional medical records by chart abstractors with substantial training in breast cancer care. All data abstracted from both conventional medical records were validated using source data verification. Source data verification was performed by a second chart abstractor, and any unresolved resulting queries were adjudicated by one of the study investigators on a case-by-case basis.

### Analysis Plan

The main purpose of this study was to characterize these 2 cohorts. Descriptive statistics were used to summarize and describe demographic information, disease characteristics, and treatment data. Comparisons between cohorts were examined using *t* tests, analysis of variance tests, and  $\chi^2$  tests as appropriate.

## Results

### Demographics

The 2 groups were well matched using initial matching criteria. Women in both groups were predominantly white (95% in both groups) and non-Hispanic (99 vs 98%). The average age of NO women was 53 years and the usual care (UC) group was 54 years (see Table 1). There were no statistically significant differences in marital status as recorded by CSS between women in the cohorts at the time of diagnosis (see Table 1). However, at time of study enrollment, a somewhat higher percentage of NO women appear to have self-reported being divorced (16% vs 8%), and more women in the UC cohort were married (66% NO vs 74% UC). These differences were not statistically significant although there was a trend ( $P = .06$ ).

### Diagnostic Status: Stage, Histological Type, Tumor Grade, Nodal and Estrogen/Progesterone/Her-2/neu Status

Most (72% of the NO cohort, and 75% of the UC cohort) of the study participants were at stage 1 or 2 when they entered the study. Although not used for matching, the women in the cohorts were also similar in histological criteria, tumor type, hormone receptor status, Her-2/neu status, and grade of primary tumors. Most had ductal carcinoma (82% and 79%, respectively). Lobular carcinoma was present in 10% of the women in both cohorts. Table 1 also shows that right- and left-sided breast cancers were approximately 50% in both cohorts. Multifocal disease was detected in 13% of NO women and 11% in the UC women. None of the women in either cohort had bilateral disease at diagnosis. Most participants had ER+ (85% and 89%, respectively) and PR+ (77% and 78%, in NO and UC women, respectively) tumors. Her-2/neu overexpression was reported in 14% of NO women and 13% of UC women. Triple-negative breast cancer was reported in 6% of NO women and 4% of UC women. None of the differences between the cohorts were statistically significant.

The tumor grade reported in pathology reports were not significantly different between the 2 groups (see Table 1). Most of the women in both groups had grade 2 tumors (39% of NO women and 42% in UC women). Grade 1 breast cancer was reported in 17% of NO women and 23% of UC women. Grade 3 tumors were reported in 17% of NO women and 23% of UC women.

Most of the women had early stage breast cancer without nodal involvement (48% for NO women compared with 54% in the UC cohort). Axillary nodal disease was more common than internal mammary lymph node disease in both cohorts (37% in NO, 38% in UC cohorts). Table 1 also

compares the number of ipsilateral level I and II axillary nodes that were positive for breast cancer cells based on the diagnostic pathology report. Of the 193 NO women, 15% had one or more malignant lymph nodes as did 18% of UC women. Again differences between the cohorts were not statistically significant.

### Breast Cancer Treatments

**Surgery.** Primary surgical treatment did not differ significantly between NO and UC women. Overall, most women had lumpectomy (57% in the NO cohort vs 51% in the UC cohort) and similar rates of mastectomy/double mastectomy (39.9% vs 46.9%; see Table 1). A similar percentage of women in both cohorts underwent removal of axillary lymph nodes (sentinel node biopsy or axillary lymph node dissection; 57% vs 52%). A small percent of women in both groups underwent a second resection in order to obtain clear surgical margins (12% and 9%, respectively). Two percent of women in both cohorts underwent prophylactic oophorectomy. Most stage 3 women underwent mastectomy regardless of cohort (77% of NO women and 79% of UC women). Few women received no surgery, 6 (3.1%) of those in the NO cohort and 7 (1.9%) of those in the UC cohort. The frequency of this did not differ between the 2 cohorts. In all cases, differences in rates between the cohorts were not statistically significant.

**Chemotherapy.** Chemotherapy was similarly used by patients in both cohorts overall. There were 6 (3.1%) women in the NO cohort and 9 (2.5%) in UC group who had recorded in the medical record that they, or a family member or guardian, refused chemotherapy that was recommended for them by their physician. The statistical frequency of this is not different between the cohorts.

Table 2 shows the 14 most commonly administered breast cancer chemotherapy drugs and utilization by stage in NO cases versus comparison women. The most commonly administered drugs were cyclophosphamide, doxorubicin, paclitaxel, and docetaxel in both cohorts. Although there were no statistically significant differences in use of various chemotherapies overall, there was a trend toward a difference between oral versus intravenous cyclophosphamide in the NO group ( $P = .07$ ; see Table 2).

### NCCN Guideline Comparisons

Overall, there were no statistically significant differences in percent of women who received standard of care surgical or adjunctive therapy that was NCCN guideline-concordant. Table 3 presents the standard recommended treatment for breast cancer stages 0 to 3 and the number and percentage of woman in the NO and UC cohorts whose actual treatment was concordant with NCCN guidelines. Most of the

**Table 1.** Baseline Characteristics of Breast Cancer Patients Who Receive Integrative Oncology (Naturopathic Oncology [NO]) Care Compared With Those Who Receive Usual Standard Care Only.<sup>a</sup>

Total, N = 553	Integrative Oncology <sup>b</sup> Cohort, n = 193	Usual Care Cohort, n = 360	$\chi^2$ , P
Race, n (%)			$\chi^2 = 2.4615$ , P = .4823
White	183 (94.8)	343 (95.3)	
Black	0 (0.0)	2 (0.6)	
Asian	7 (3.6)	13 (3.6)	
Mixed	3 (1.6)	2 (0.6)	
Ethnicity, n (%)			$\chi^2 = 0.350$ , P = .5540
Hispanic	2 (1.0)	6 (1.7)	
Non-Hispanic	191 (99.0)	354 (98.3)	
Age at enrollment, mean (SD)	53 (11.2)	54 (10.3)	
Marital status at diagnosis, n (%)			$\chi^2 = 5.862$ , P = .3198
Married	128 (66.3)	267 (74.2)	
Divorced	18 (9.3)	25 (6.9)	
Single	31 (16.1)	36 (10.0)	
Widowed	2 (1.0)	4 (1.1)	
Unmarried or domestic partner	4 (2.1)	8 (2.2)	
Unknown	10 (5.2)	20 (5.6)	
Stage, n (%)			$\chi^2 = 5.321$ , P = .3780
Stage 0	20 (10.4)	30 (8.3)	
Stage 1	62 (32.1)	142 (39.4)	
Stage 2	77 (39.9)	128 (35.6)	
Stage 3	26 (13.5)	48 (13.3)	
Stage 4	7 (3.6)	7 (1.9)	
Unknown	1 (0.5)	5 (1.4)	
Histology, n (%)			$\chi^2 = 1.665$ , P = .6448
Ductal	158 (81.9)	284 (78.9)	
Lobular	19 (9.8)	35 (9.7)	
Mixed	16 (8.3)	40 (11.1)	
Unknown	0 (0.0)	1 (0.3)	
Laterality, n (%)			$\chi^2 = 0.0398$ , P = .8419
Tumor on left	98 (50.8)	186 (51.7)	
Tumor on right	95 (49.2)	174 (48.3)	
Bilateral or midline tumor	0 (0.0)	0 (0.0)	
Estrogen/progesterone receptor, HER-2/neu overexpression, n (%)			
ER+	164 (85.0)	320 (88.9)	NS
PR+	148 (76.7)	279 (77.5)	NS
Her2+	27 (14.0)	49 (13.6)	NS
Triple negative	12 (6.2)	14 (3.9)	NS
Grade, n (%)			$\chi^2 = 5.713$ , P = .1264
Grade 1	33 (17.1)	81 (22.5)	
Grade 2	75 (38.9)	151 (41.9)	
Grade 3	83 (43.0)	121 (33.6)	
Grade unknown	2 (1.0)	7 (1.9)	
Internal/axillary lymph nodes, multifocal, n (%)			
Internal nodes present	2 (1.0)	2 (0.6)	NS
Axillary nodes present	72 (37.3)	136 (37.8)	NS
Multifocal tumor	25 (12.9)	38 (10.6)	NS

(continued)

Table 1. (continued)

Total, N = 553	Integrative Oncology <sup>b</sup> Cohort, n = 193	Usual Care Cohort, n = 360	$\chi^2$ , P
Number of positive ipsilateral level I to II axillary lymph nodes, n (%)			$\chi^2 = 8.326, P = .3047$
0 nodes	93 (48.2)	195 (54.2)	
Nodes not examined, not found, or not removed	18 (9.3)	19 (5.3)	
Positive aspiration only	11 (5.7)	10 (2.8)	
1 node	29 (15.0)	64 (17.8)	
2 nodes	10 (5.2)	20 (5.5)	
3 nodes	13 (6.7)	17 (4.7)	
4 nodes	3 (1.6)	5 (1.4)	
5+ nodes	16 (8.3)	30 (8.3)	
Type of surgery, n (%)			$\chi^2 = 6.180, P = .1861$
No surgery	6 (3.1)	7 (1.9)	
Lumpectomy or excisional biopsy	110 (56.9)	184 (51.1)	
Mastectomy	56 (29.0)	119 (33.0)	
Bilateral mastectomy	21 (10.9)	50 (13.9)	
Chemotherapy and radiotherapy received, n (%)			
Radiotherapy	118 (61.1)	203 (56.4)	NS
Chemotherapy	106 (54.9)	175 (48.6)	NS

<sup>a</sup>Demographic, diagnostic, and treatment data for 193 women with breast cancer who received outpatient integrative oncology services compared with a matched comparison cohort of 360 women with breast cancer who received usual oncologic care for their breast cancer. All data are from the Western Washington Cancer Surveillance System.

<sup>b</sup>Integrative Oncology (IO) is synonymous with Naturopathic Oncology (NO)

women in both cohorts (71% of NO women and 70% of UC cohort women) received surgical, radiotherapy, and chemotherapy that met NCCN recommendations. Surgical therapies were 94% to 100% concordant with NCCN recommendations for stage 0, 1, 2, and 3 breast cancer. The most common reasons for nonconcordance with the NCCN guidelines were related to differences in radiotherapy. Although the overall rates of use were similar, it appears that more women with ductal carcinoma in situ (stage 0) received radiotherapy in the UC group (85%) compared with the NO group (64%). Again, it appears that more women in the UC cohort with stage 3 breast cancer (N = 46) received radiotherapy (69%) compared with stage 3 women in the NO cohort (N = 26) who received radiotherapy (46%). This difference was not statistically different.

**Mastectomy and Radiotherapy.** A similar percentage of women in both cohorts with breast cancer elected to receive a mastectomy as primary surgical treatment. However, fewer women in the NO cohort with stage IIIA breast cancer who received a mastectomy (N = 9) also received radiotherapy (67%) compared with 79% of stage IIIA women in the UC cohort (N = 29). In stage IIIB and IIIC patients, only 50% of women in the NO cohort who received a mastectomy (N =

12) also underwent radiotherapy compared with similarly staged women in the UC cohort (N = 14; 71%). Again, because of the small sample size, these differences were not statistically different.

**Antiestrogen Hormone Therapy.** Table 4 shows the specific antiestrogen drugs used by women in both cohorts overall as recorded in their charts and abstracted. The most common drugs used by both cohorts were tamoxifen, arimidex, letrozole, and aromasin. In the subsample of women who were estrogen positive (164 in the NO cohort and 320 in the UC cohort), use of any antiestrogen adjunctive therapy differed between the cohorts (72% vs 84%, respectively;  $P < .01$ ). Use of any of the antiestrogens also appears to be lower among the NO cohort compared with the UC cohort overall when CSS data were used for the comparison, which showed a trend toward significance (Pearson's  $\chi^2$  test  $P = .052$ ).

## Conclusions

Breast cancer patients in the UC comparison group were well matched with NO cases with regard to demographics, stage, grade, laterality, histological, and biological

**Table 2. Types of Chemotherapy Drugs<sup>a</sup> (N = 472).**

Type of Chemotherapy	Stage 0		Stage 1		Stage 2		Stage 3		Stage 4		Stage Unknown		Total	
	IO Cohort, n (%)	UC Cohort, n (%)	IO Cohort, n (%)	UC Cohort, n (%)	IO Cohort, n (%)	UC Cohort, n (%)	IO Cohort, n (%)	UC Cohort, n (%)	IO Cohort, n (%)	UC Cohort, n (%)	IO Cohort, n (%)	UC Cohort, n (%)	IO Cohort, n (%)	UC Cohort, n (%)
Capecitabine (Xeloda)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)	2 (2.0)	1 (4.2)	3 (6.7)	2 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	5 (1.7)
Carboplatin (Paraplatin)	0 (0.0)	0 (0.0)	5 (8.6)	9 (12.8)	10 (10.2)	3 (12.5)	5 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	17 (9.4)	24 (8.2)
Cisplatin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
Cyclophosphamide (Cytospan) <sup>IV</sup>	0 (0.0)	0 (0.0)	11 (19.0)	36 (51.4)	59 (60.2)	18 (75.0)	38 (84.4)	7 (70.0)	3 (37.5)	0 (0.0)	2 (100.0)	2 (100.0)	72 (40.0)	121 (41.4)
Cyclophosphamide (Cytospan)- Oral	0 (0.0)	0 (0.0)	5 (8.6)	7 (10.0)	4 (4.1)	3 (12.5)	3 (6.7)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	16 (8.9)	8 (2.7)
Docetaxel (Taxotere)	0 (0.0)	0 (0.0)	12 (20.7)	23 (32.9)	36 (36.7)	6 (25.0)	12 (26.7)	3 (30.0)	1 (12.5)	0 (0.0)	1 (50.0)	1 (50.0)	44 (24.4)	71 (24.3)
Doxorubicin (Adriamycin)	0 (0.0)	0 (0.0)	2 (3.4)	5 (4.2)	23 (32.9)	19 (79.2)	34 (75.5)	5 (50.0)	2 (25.0)	0 (0.0)	1 (50.0)	1 (50.0)	49 (27.2)	77 (26.4)
Doxorubicin, pegylated (Doxil)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.3)
Lapatinib (Tykerb)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	1 (2.2)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.0)
Methotrexate (Trexall)	0 (0.0)	0 (0.0)	5 (8.6)	7 (10.0)	5 (5.1)	0 (0.0)	2 (4.4)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (7.2)	9 (3.1)
Paclitaxel (Taxol)	0 (0.0)	0 (0.0)	5 (8.6)	11 (9.3)	33 (33.7)	18 (75.0)	29 (64.4)	6 (60.0)	4 (50.0)	0 (0.0)	1 (50.0)	1 (50.0)	55 (30.6)	78 (26.7)
Paclitaxel, protein-bound (Abraxane)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	5 (5.1)	1 (4.2)	3 (6.7)	2 (20.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	10 (3.4)
Vinorelbine (Navelbine)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.0)	1 (4.2)	1 (2.2)	3 (30.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	4 (1.4)
5-FU (Adrucil/Carac/Efudex/ Fluoroplex)	0 (0.0)	0 (0.0)	5 (8.6)	8 (11.4)	5 (5.1)	0 (0.0)	3 (6.7)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	14 (7.8)	9 (3.1)

Abbreviations: IO, integrative oncology; UC, usual care; 5-FU, fluorouracil.

<sup>a</sup>Types of chemotherapy drugs administered to 180 women with breast cancer who receive outpatient IO services compared with a matched comparison cohort of 292 women with breast cancer who received usual oncologic care for their breast cancer. Data are from the Western Washington Cancer Surveillance System (CSS) and abstracted medical records (REDCap). Includes all IO and usual care cohort patients eligible for abstraction as of January 1, 2015, for whom a CSS record was available and a completed clinical status electronic case report form was entered into REDCap for both enrollment and 6 months. Stage was abstracted from the patient's medical record at study enrollment. If that was not available, then the CSS stage at diagnosis was used if time from diagnosis to enrollment <2 years.

**Table 3.** NCCN Treatment Recommendation Concordance Based on 27 Quality Measures<sup>a,12</sup>

Condition/ tx nbr	Stage	Condition	Treatment  NCCN Recommended Treatment Based on 27 Quality Controls tx	IO Cohort, N = 193		UC Cohort, N = 360	
				N	Compliant, N (%)	N	Compliant, N (%)
1	Clinical stage 0 breast cancer	DCIS	Lumpectomy or mastectomy	18	17 (94.4)	22	21 (95.5)
2			NO chemotherapy	18	17 (94.4)	22	21 (95.5)
3		DCIS, treated with lumpectomy	Whole breast RT	14	9 (64.3)	13	11 (84.6)
4			NO ALNS	14	13 (92.8)	13	8 (61.5)
5		DCIS, treated with mastectomy	NO whole breast RT	3	2 (66.7)	8	8 (100.0)
1A	Non-DCIS	Non-DCIS	Lumpectomy or mastectomy	2	2 (100.0)	8	8 (100.0)
2A			NO chemotherapy	2	2 (100.0)	8	8 (100.0)
3A		Non-DCIS, treated with lumpectomy	Whole breast RT	2	2 (100.0)	6	4 (66.7)
4A			NO ALNS	2	2 (100.0)	6	6 (100.0)
5A		Non-DCIS, treated with mastectomy	NO whole breast RT	0	0 (0.0)	2	2 (100.0)
6	Clinical stage I and II breast cancer	Invasive breast cancer	Lumpectomy or mastectomy	139	138 (99.3)	270	270 (100.0)
7			Treated with lumpectomy	Whole breast RT	85	68 (80.0)	142
8		Treated with lumpectomy	ALNS	85	84 (98.8)	142	141 (99.3)
9			Treated with mastectomy, $\geq 4$ nodes positive	Chest wall RT	1	0 (0.0)	2
10		Treated with mastectomy, tumor >5 cm	ALNS	1	1 (100.0)	2	2 (100.0)
11			Chest wall RT	3	1 (33.3)	2	2 (100.0)
12		Treated with mastectomy, nodes negative and tumor $\leq 5$ cm	ALNS	3	3 (100.0)	2	2 (100.0)
13			NO chest wall RT	25	23 (92.0)	73	64 (87.7)
14		Treated with surgery, ductal, lobular, mixed, or metaplastic histology; nodes negative and tumor $\leq 0.5$ cm/microinvasive	ALNS	25	25 (100.0)	73	73 (100.0)
15			NO chemotherapy	6	4 (66.7)	22	21 (95.5)
16		Treated with surgery, tubular, or colloid histology; nodes negative and tumor $\leq 1$ cm	NO chemotherapy	1	0 (0.0)	2	2 (100.0)
17		Treated with surgery, tubular, or colloid histology; nodes negative and tumor >3 cm	Chemotherapy	0	0 (0.0)	0	0 (0.0)
18		Treated with surgery; ductal, lobular, mixed, or metaplastic histology; nodes negative; tumor 0.6 to 1.0 cm; well differentiated and no unfavorable features	NO chemotherapy	4	3 (75.0)	12	12 (100.0)
19		Treated with surgery; ductal, lobular, mixed, or metaplastic histology; nodes negative and tumor >1 cm; HR negative	Chemotherapy	48	20 (41.7)	69	24 (34.8)
20		Treated with surgery; ductal, lobular, mixed, or metaplastic histology; nodes negative and tumor 1.1 to 3 cm; HR positive	Chemotherapy	8	7 (87.5)	14	11 (78.6)
21		Treated with surgery; ductal, lobular, mixed, or metaplastic histology; nodes negative and tumor >3 cm; HR positive	Chemotherapy	1	1 (100.0)	1	1 (100.0)
22		Treated with surgery; nodes positive; HR negative	Chemotherapy	34	25 (73.5)	66	44 (66.7)
23		Treated with surgery; nodes positive; HR positive	Chemotherapy	9	9 (100.0)	14	12 (85.7)

(continued)



Table 3. (continued)

Condition/ tx nbr	Stage	Condition	Treatment	IO Cohort, N = 193		UC Cohort, N = 360	
			NCCN Recommended Treatment Based on 27 Quality Controls tx	N	Compliant, N (%)	N	Compliant, N (%)
24	Clinical stage III breast cancer	Stage IIIA treated with mastectomy	Chemotherapy	9	9 (100.0)	29	29 (100.0)
25			RT	9	6 (66.7)	29	23 (79.3)
24A		All other stage III	Chemotherapy	12	9 (75.0)	14	13 (92.8)
25A			RT	12	6 (50.0)	14	10 (71.4)
26		Stage IIIB	Neoadjuvant chemotherapy	2	2 (100.0)	3	2 (66.7)
27		Stage IIIB	Anthracycline chemotherapy	5	5 (100.0)	5	5 (100.0)
Study patients not included in above criteria							
Stage IV					7		7
Stage unknown					1		5
All treatment							
				N		Percent	
				Compliant	Noncompliant	Total	Noncompliant
Cohort 1A				131	54	185	29.2
Cohort 2				245	103	348	29.6
Undertreatment							
				N		Percent	
				Compliant	Noncompliant	Total	Noncompliant
Cohort 1A				137	48	185	25.9
Cohort 2				251	97	348	27.9
Overtreatment							
				N		Percent	
				Compliant	Noncompliant	Total	Noncompliant
Cohort 1A				178	7	185	3.8
Cohort 2				342	6	348	1.7

Abbreviations: IO, integrative oncology; UC, usual care; NCCN, National Comprehensive Cancer Network; DCIS, ductal carcinoma in situ; NO, naturopathic oncology; RT, radiation therapy; ALNS, axillary lymph node surgery; HR, hormone receptor.

<sup>a</sup>All data are from CSS. Cells shaded gray represent data for breast cancer treatment (tx) considered to be overtreatment. All other data represent tx considered necessary to avoid undertreatment. The N for Condition/tx nbr 26 and 27 are different due to patients excluded for unknown neoadjuvant tx. Unfavorable features include angiolymphatic invasion, high nuclear grade, high histology grade, and HER-2 overexpression.

features of breast cancer at time of study enrollment. Extent of nodal disease at diagnosis was similar between the cohorts. Similar surgical and chemotherapy treatments were used in both the cohorts. Most women in both cohorts received NCCN guideline-adherent primary oncologic treatment for their breast cancer. However, it appears that fewer women in the adjunctive NO cohort received radiotherapy compared with the usual care cohort although differences are not statistically significant. Women with ER+ breast cancer who received integrative oncology care were also less likely to receive antiestrogen therapy.

NO care is generally added to, and is not substituted for, conventional oncology treatment. Our results agree with Lafferty's group<sup>13,14</sup> who studied cancer care across organ sites based on insurance data, and which has also reported that in western Washington State, CAM care is rarely used instead of conventional care.

There are several limitations to this study. Investigators attempted to minimize bias in the study population by recruiting participants from naturopathic physicians with board certification in NO practicing within a SEER catchment area in a state where NDs are licensed physicians. However, the majority of the NO participants were

**Table 4.** Differences in Antiestrogen Use.

Antiestrogen	Cohorts	
	NO Care, N = 192, n (%)	Conventional Care, N = 359, n (%)
Anastrozole (Arimidex)	55 (28.6)	131 (36.5)
Evista	0 (0.0)	1 (0.3)
Exemestane (Aromasin)	17 (8.8)	32 (8.9)
Fulvestrant (Faslodex)	2 (1.0)	2 (0.6)
Letrozole (Femara)	29 (15.1)	60 (16.7)
Lupron (Leuprorelin)	11 (5.7)	10 (2.8)
Tamoxifen (Nolvadex)	69 (35.9)	157 (43.7)
Toremifene	0 (0.0)	1 (0.3)
Zoladex (Goserelin)	1 (0.5)	3 (0.8)
Used any antiestrogen <sup>a</sup>	123 (64.1)	272 (75.8)

<sup>a</sup>Statistically significant difference for any use of an antiestrogen versus no recorded use. Pearson's  $\chi^2$  test with Yates' continuity correction;  $\chi^2 = 7.8755$ , degrees of freedom = 1,  $P < .01$ .

recruited through 1 of the 6 recruitment sites, which may affect the conclusions of this study. These results may have been different had we recruited either from NDs with the FABNO designation practicing in another licensed state or in a state where there is no licensure for NDs to practice medicine. The participant population may also differ in states that do not have an Every Category of Provider law or similar legislation ensuring coverage for NO care.

Residents of Western Washington State and in particular the Puget Sound Region are generally white, well educated, and enjoy a high standard of living, and those seeking NO care may be even more so. The effects of socioeconomic status on disparities in cancer care, including access to health care, insurance coverage, expression of prognostic factors, and earlier stage at presentation and treatment choices, have been well documented. Women living in this region who chose to participate in this study may therefore enjoy the advantages of the socioeconomic status and are accordingly have been more willing to accept conventionally recommended treatments.

This ongoing longitudinal observational study will be able to provide quality data on clinical and other outcomes for women receiving breast cancer treatment who do and do not use adjunctive NO allowing for comparison of the outcomes of the 2 cohorts. This study is part of a larger effort to determine cost effectiveness of NO care for women with breast cancer.

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The views expressed in this article are the contributing authors' own and not an official position of the institution or funder. Study data were collected and managed using REDCap electronic data capture tools hosted at Bastyr University.

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### ORCID iDs

Erin Sweet  <https://orcid.org/0000-0003-4840-6125>

M. Robyn Andersen  <https://orcid.org/0000-0002-6083-4619>

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