



# The association of socioeconomic status with receipt of neoadjuvant chemotherapy

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## Abstract

**Background** There are advantages to neoadjuvant chemotherapy in operable breast cancer, particularly for those with higher-risk cancers, but little is known about factors that are associated with the use of neoadjuvant chemotherapy outside of clinical trials. We examined whether use of neoadjuvant chemotherapy instead of adjuvant chemotherapy varies by nonclinical factors such as patient socioeconomic status or rural residence.

**Methods** Women diagnosed with breast cancer in 2013–2014 at eight medical institutions were surveyed by mail regarding their experiences with breast cancer treatment, and this information was linked to hospital-based cancer registries. We examined the use of neoadjuvant chemotherapy among women with histologically confirmed invasive stage I–III breast cancer and used regression models to examine the association of socioeconomic status with chemotherapy timing. We also explored potential mechanisms for those differences.

**Results** Over 29% of the chemotherapy sample overall received neoadjuvant chemotherapy. Neoadjuvant receipt was lower for those with income < \$100,000 (AOR 0.56, 95% CI 0.2–0.9) even with adjustment for other demographics, stage, and biomarker status, and findings for education and a variable for both lowest education and income < \$100,000 were similar. Rural/urban residence was not associated with neoadjuvant receipt. Differences by income in perceptions of the importance of neoadjuvant chemotherapy advantages and disadvantages did not appear to explain the differences in use by income.

**Conclusions** In a multicenter sample of breast cancer patients, lower income was strongly associated with less receipt of neoadjuvant chemotherapy. Since patients with lower socioeconomic status are more likely to present with later-stage disease, this pattern has the potential to contribute to breast cancer outcome disparities.

**Keywords** Breast cancer · Disparities · Neoadjuvant chemotherapy · Socioeconomic status

## Background

The improvement in breast cancer survival conferred by chemotherapy is the same whether it is delivered before definitive surgery (neoadjuvant) or after (adjuvant) [1, 2]. There are advantages to neoadjuvant treatment, however, particularly for certain groups of patients. For patients with larger cancers or smaller breast size, neoadjuvant chemotherapy increases the likelihood of successful breast conservation and can make inoperable disease resectable [3]. Furthermore, unlike adjuvant chemotherapy, neoadjuvant chemotherapy both predicts prognosis and allows assessment of treatment response, and therefore has the potential to alter the course of treatment. This information about treatment response and prognosis is especially important for patients with higher recurrence risk, and guidelines by the

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National Comprehensive Cancer Network (NCCN) recommend considering neoadjuvant chemotherapy for women with Stage 2 cancer or above [3].

Given these advantages, neoadjuvant chemotherapy is now used in some sites for up to a quarter of breast cancer patients receiving chemotherapy [1, 2, 4]. However, its use varies substantially even between large centers [4–8]. Research into adoption of other new medical technologies has shown that adoption often varies strongly by nonclinical factors, including patient socioeconomic status. Variation by socioeconomic status would be a particular concern in breast cancer care. On average, patients with lower socioeconomic status have higher-stage breast cancers [9] and therefore have a greater chance of benefitting from neoadjuvant therapy.

Variation in use of neoadjuvant chemotherapy could also stem from differences in patient preferences. There appear to be few disadvantages of neoadjuvant chemotherapy, but care may appear more complex to the patient, and patients may find the delay to surgical excision concerning [10]. Little is known about patients' experiences with neoadjuvant compared with adjuvant chemotherapy, the value patients place on the advantages and disadvantages of neoadjuvant timing of chemotherapy, or whether these might vary by socioeconomic status. To address these gaps, we examined a sample of women with breast cancer who participated in a cross-sectional multicenter study at eight centers and received chemotherapy, examining patterns of chemotherapy timing (neoadjuvant vs adjuvant) by socioeconomic status. We also describe patients' experiences with neoadjuvant compared with adjuvant chemotherapy, including their perceptions of the risks/benefits, the decision-making process, and quality of care.

## Methods

### Study source and population

The study was performed within the Greater Plains Collaborative (GPC), one of 13 Patient Centered Outcomes Research network (PCORnet) clinical data research networks (CDRNs). The study sample included eight GPC sites (of a total of nine that treated adult breast cancer patients) from seven Midwestern states. In brief, each center extracted data from their North American Association of Central Registries-formatted tumor registry into its Informatics for Integrating Biology and the Bedside (i2b2) system, and women aged 18 or older with a first diagnosis of histologically confirmed Stage 0–3 breast cancer made between 1/1/2013 and 5/1/2014 were identified. A random sample of 250 of these women from each site was then selected for a mailed survey sent in May 2015, with up to 10 replacements for any surveys that were returned with evidence that a subject was

ineligible (subject died, mailing was returned by the postal service unopened, or subject reported that the 2013–2014 breast cancer was not her first breast cancer). In addition to the survey, all subjects were asked for additional consent for investigators to examine their medical records, including information from the tumor registry. The study was approved and monitored by the Institutional Review Board (IRB) at the coordinating center (University of Iowa) with the other centers ceding review.

Patients were asked in the survey to report timing of their chemotherapy, specifically whether they had chemotherapy before surgery only (neoadjuvant), after surgery only (adjuvant), or both before and after surgery. Prior studies suggest that patient self-report of chemotherapy is highly consistent with other measures, including administrative (billing) data [11]. Subjects with invasive (stage 1–3) breast cancer who reported having received either neoadjuvant or adjuvant chemotherapy were eligible for this study. Because extent of disease is important in cancer treatment decision-making, only those women who also agreed to use of tumor registry information were included in the final sample.

### Variable definitions

Subject demographics (age, race/ethnicity, education, employment, income, and marital status) were obtained from survey responses. Rural residence was identified using the rural–urban continuum categories from 2013 US Census data for the subject's zip code. Extent of disease (stage) and tumor markers [hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2)] were obtained from cancer registry data.

Three Likert-scaled items were also developed for the survey regarding the importance patients placed on the advantages and disadvantages of neoadjuvant versus adjuvant chemotherapy. These items were based on summary statements from physician treatment guidelines [3] and used wording that was similar to previously developed items regarding importance of factors in breast cancer treatment decision-making [12]. Participants responded to “When decisions were being made about chemotherapy, how important was it that the timing of the chemotherapy (before or after surgery or both)....(a) .....would allow you to know that your cancer had shrunk; (b) .....would improve your chances of having a lumpectomy; and (c) .....would make sure the cancer was removed by surgery as soon as possible” with 5 response levels, with labels below the first as “not at all important” the third “somewhat important” and the last “very important.”

Patient experiences with decisions related to chemotherapy were assessed using several measures. To assess subjects' reports of shared decision-making, we utilized two instruments with Likert-scaled items, [13] the first of which

evaluated patients' preferred participation in breast cancer treatment decisions by asking "Which of the following best describes the way you would prefer to make a decision about your cancer treatment?" with five responses ranging from "I prefer that I make the decisions about treatment with little or no input from my doctors" to "I prefer that my doctors make the decision about treatment with little or no input from me." The second instrument then asked about subjects' actual experiences specific to the chemotherapy with responses substituting, for example, 'I made' for 'prefer that I make' [13, 14]. Using an adaptation of the actual experience item, subjects were also asked about family participation in the decision.

Patient-reported experiences with quality of physician communication (2 items) and coordination of care (6 items) were measured through Likert-scaled items based on the Consumer Assessment of Health Care Providers and Systems. These items were previously used in a longer measure of patient-perceived quality of cancer care [15, 16] and are strongly correlated with overall perceptions of quality of care [16].

## Analysis

Subjects who reported that they had chemotherapy both before and after surgery ( $n = 4$ ) were not included in the study. Because of relatively high missingness of information for variables for both HER2 status and income, missing categories were created for all variables.

Initial examination of the overall sample showed that there was no association of education or income with overall rates of chemotherapy use. Furthermore, few African-American or Hispanic women were treated for breast cancer at our study sites. We thus focused our examination on the potential association of neoadjuvant chemotherapy use (vs adjuvant chemotherapy use) with socioeconomic status as measured by education and income. In a bivariate examination of the association of income with neoadjuvant receipt, there were no differences between the lowest five groups we examined, so in further analyses they were classified as highest income ( $> \$100,000$ ) versus all others. In bivariate examination of the association of education with neoadjuvant receipt, there were no difference in neoadjuvant receipt in the highest three groups we examined, so in further analyses they were classified as lowest group (high school/GED or less) vs all others. Our primary analyses included either income or education examined in a regression model which included tumor markers, stage, and demographic variables. To examine the robustness of these results, we also examined several alternate models of SES: a model with both education and income included together, and one using a variable which combined income and education into four groups: Less than \$100,000 and high school or less, less than

\$100,000 and more than high school, greater than \$100,000 and high school or less, and greater than \$100,000 and more than high school. Finally, we examined the inclusion of a measure of health literacy [17, 18] which in models with education was not statistically significant, so was removed from further analyses.

We also examined subjects' beliefs/preferences and experiences with care (importance of neoadjuvant chemotherapy advantages/disadvantages, decision-making roles, and perceived quality of care) by timing of chemotherapy. Results for the new variables for importance of neoadjuvant advantages/disadvantages were examined either in three categories (1–2, 3 and 4–5) or dichotomized with 1–3 versus 4–5; results were similar so the two-category variable was used. Following Sulayman, decision-making variables were recategorized as passive, shared, and active [14].

Finally, we performed exploratory analyses examining whether differences in patients' beliefs and/or experiences were mechanisms for the association of income and education with chemotherapy timing. Based on unadjusted findings for the association of perceptions of neoadjuvant chemotherapy advantages/disadvantages with chemotherapy timing, we examined this relationship in adjusted models, as well as whether any differences by income in perceptions of advantages might explain differences in receipt of neoadjuvant chemotherapy. All analyses were conducted with SAS statistical software, version 9.4 (SAS Institute, Cary, NC) and two-tailed  $p$  values.

The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Results

The overall sample of 1235 subjects and the details of the calculation of survey response rates (overall response rate 62.2%) have been previously described [19]. Among the 877 survey respondents who provided consent to view their cancer registry information, 331 received either neoadjuvant or adjuvant chemotherapy and were included in further analyses. About 40% of this sample was age 50 or under, 19.9% had a high school education or less, and 29.2% had a household income that was less than \$50,000 yearly. As shown in Table 1, 29.6% of the women ( $n = 98$ ) received neoadjuvant chemotherapy.

### Factors associated with neoadjuvant chemotherapy

Receipt of neoadjuvant chemotherapy among the chemotherapy sample (i.e., only patients who received chemotherapy) varied substantially by age, tumor markers, and extent of disease, so that 50% of HR– and HER2+ received

**Table 1** Characteristics of stage 1–3 patients who received chemotherapy

	Neoadjuvant (N=98)	Adjuvant (N=233)	Total (N=331)	p value (neoadjuvant compared with adjuvant)
Age (mean, SD)				<0.001
25–40	25 (25.8%)	20 (8.6%)	45 (13.6%)	
41–50	27 (27.8%)	59 (25.3%)	89 (26.1%)	
51–60	27 (27.8%)	87 (37.3%)	114 (34.6%)	
61–80	18 (18.6%)	67 (28.8%)	85 (25.8%)	
Missing	1 (1.0%)	0 (0.0%)	1 (0.3%)	
Race				0.60
White	89 (90.8%)	219 (94.0%)	308 (93.1%)	
Black	7 (7.1%)	9 (3.9%)	16 (4.8%)	
American Indian, Aleutian, or Eskimo	0 (0.0%)	1 (0.43%)	1 (0.30%)	
Chinese	0 (0.0%)	2 (0.86%)	2 (0.60%)	
Other Asian	1 (1.0%)	1 (0.43%)	2 (0.60%)	
Missing	1 (1.0%)	1 (0.43%)	2 (0.60%)	
Marital status				0.78
Partnered	73 (74.5%)	177 (76.0%)	250 (75.5%)	
Unpartnered	25 (25.5%)	56 (24.0%)	81 (24.5%)	
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Currently employed	66 (67.4%)	164 (70.4%)	230 (69.5%)	0.55
Missing	0 (0.0%)	1 (0.4%)	1 (0.30%)	
Yearly household income				0.03
Less than \$100,000	54 (55.1%)	164 (70.4%)	218 (65.9%)	
Greater than \$100,000	30 (30.6%)	48 (20.6%)	78 (23.6%)	
Missing/prefer not to answer	14 (14.3%)	21 (9.0%)	35 (10.6%)	
Education				0.02
High school/GED or less	12 (12.4%)	54 (23.2%)	66 (19.9%)	
At least some college	86 (87.8%)	177 (80.0%)	263 (79.5%)	
Missing/prefer not to answer	0 (0.0%)	2 (0.86%)	2 (0.6%)	
Rural (nonmetropolitan statistical area)	18 (18.4%)	60 (25.8%)	78 (23.6%)	0.15
Stage				0.02
1	15 (15.3%)	93 (39.9%)	108 (32.6%)	
2	59 (60.2%)	104 (44.6%)	163 (49.2%)	
3	24 (24.5%)	36 (15.5%)	60 (18.1%)	
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	
HER2/HR status				0.008
HER2+/HR+	22 (22.5%)	33 (14.2%)	55 (16.6%)	
HER2+/HR–	10 (10.2%)	10 (4.3%)	20 (6.0%)	
HER2–/HR+	43 (43.9%)	146 (62.7%)	189 (57.1%)	
HER2–/HR–	20 (20.4%)	37 (15.9%)	57 (17.2%)	
Missing	3 (3.1%)	7 (3.0%)	10 (3.0%)	
GPC site				0.16
1	13 (13.3%)	26 (11.2%)	39 (11.8%)	
2	5 (5.1%)	20 (8.6%)	25 (7.6%)	
3	12 (12.2%)	22 (9.4%)	34 (10.3%)	
4	9 (9.2%)	34 (14.6%)	43 (13.0%)	
5	10 (10.2%)	29 (12.5%)	39 (11.8%)	
6	14 (14.3%)	38 (16.3%)	52 (15.7%)	
7	24 (24.5%)	31 (13.3%)	55 (16.6%)	
8	11 (11.2%)	33 (14.2%)	44 (13.3%)	

All variables measured at time of diagnosis

neoadjuvant chemotherapy compared with 22.8% of those with HR+ and HER2– (Table 1). Neoadjuvant chemotherapy receipt ranged from a low of 13.8% for those with Stage 1 cancer to 40.0% for those with Stage 3 disease. Although differences in use of neoadjuvant chemotherapy by site of care were not statistically significant, there was substantial site-to-site variation, from a low of 20.0% of chemotherapy given as neoadjuvant at one site, to a high of 43.6%.

Use of neoadjuvant chemotherapy among those receiving chemotherapy also varied substantially by income and education (Table 1), so that 41.9% of patients with household income (> \$100,000 (approximately the highest quartile) received neoadjuvant chemotherapy. Only 18.2% of those with a high school education or less received neoadjuvant chemotherapy versus 32.7% of those with at least some college. While women residing in rural zip codes were less likely than those in urban zip codes (i.e., zip codes in metropolitan statistical areas) to receive neoadjuvant chemotherapy, this difference was not statistically significant.

In models adjusted for demographics, stage, and biomarker status, patients with lower household income were only slightly more than half as likely (OR 0.56, 95% CI 0.2–0.9) as those with income > \$100,000 to receive neoadjuvant chemotherapy (Table 2). The differences in neoadjuvant use by education that were seen in unadjusted analyses

(Table 1) were no longer significant in adjusted analyses of education alone ( $p=0.15$ ) or analyses that included both income and education. When income and education were combined into four categories (see analysis), neoadjuvant use by those with low income/low education differed from other categories, but no other differences were found (data not shown).

### Patient experiences with and preferences regarding chemotherapy

Patient reports of beliefs/preferences and experiences regarding chemotherapy are shown by timing of chemotherapy in Table 3. Subjects who received neoadjuvant chemotherapy differed from those with adjuvant chemotherapy in their response to two of three questions about the importance of specific advantages and disadvantages of neoadjuvant chemotherapy. Women who received neoadjuvant chemotherapy were more likely than those who received adjuvant to report that “know(ing) the cancer had shrunk” was important (4–5 on a Likert scale of 1–5) and less likely to report that “making sure the tumor was removed by surgery as soon as possible” was important. Women who received neoadjuvant chemotherapy were slightly more likely to report that “increasing the chances for lumpectomy” were important,

**Table 2** Multivariable analysis of association of neoadjuvant chemotherapy use with nonclinical and clinical characteristics

	Unadjusted [OR (CI 95%)]	<i>p</i> value	Adjusted [OR (CI 95%)]	<i>p</i> value
Age		0.0004		0.01
25–40	4.7 (2.1–10.2)		3.8 (1.6–9.0)	
41–50	1.7 (0.8–3.4)		1.7 (0.8–3.6)	
51–60	1.2 (0.6–2.3)		1.2 (0.6–2.5)	
61–80	–		–	
Marital status				0.16
Partnered	0.08 (0.6–1.9)		0.6 (0.3–1.2)	
Unpartnered	–		–	
Stage		0.0001		0.0001
1	0.2 (0.1–0.5)		0.2 (0.1–0.44)	
2	0.9 (0.5–1.6)		0.7 (0.4–1.4)	
3	–		–	
Subtype		0.009		0.007
HER2– HR–	1.8 (1.0–3.5)		2.2 (1.1–4.6)	
HER2+ HR+	2.3 (1.2–4.3)		2.5 (1.2–5.0)	
HER2+ HR–	3.4 (1.3–8.7)		4.3 (1.4–12.7)	
HER2– HR+	–		–	
Income		0.03		0.01
Missing	1.07 (0.5–2.4)		1.4 (0.6–3.5)	
Less than \$100,000	0.53 (0.3–0.9)		0.56 (0.2–0.9)	
Greater than \$100,000	–		–	
Rural (nonmetropolitan statistical area)	0.65 (0.4–1.2)	0.15	0.81 (0.4–1.6)	0.54

**Table 3** Association of chemotherapy timing with preferences, shared decision-making, and perceived quality of care

	Neoadjuvant (N=98)	Adjuvant (N=233)	p value
Shared decision-making—general (n=332)			0.22
Active: I make decision with little input from doctor <i>or</i> I make decision after considering doctor opinion	22 (22.6%)	67 (28.8%)	
Make decision on equal basis	47 (48.5%)	118 (50.6%)	
Passive: Doctor makes decision and considers my opinion <i>or</i> Doctor makes decision with little input from me	28 (28.9%)	48 (20.6%)	
SDM actual—chemotherapy			0.06
Active: I make decision with little input from doctor/I I make decision after considering doctor opinion	19 (19.4%)	70 (30.0%)	
Make decision on equal basis	46 (47.0%)	108 (46.4%)	
Passive: Doctor make decision and consider my opinion/Doctor make decision with little input from me	33 (37.7%)	55 (23.6%)	
Quality of communication (mean, SD) (n=331)	7.2 (1.03)	7.3 (1.11)	0.57
Quality of care coordination (mean, SD) (n=330)	21.6 (2.5)	21.5 (2.7)	
When decisions were being made about chemotherapy, how important was it that the timing of the chemotherapy (before or after surgery or both) <sup>a</sup>			
Would allow you to know that your cancer had shrunk (n=303)			<0.001
Not important to somewhat important	8 (8.3%)	94 (45.4%)	
Important or very important	88 (91.7%)	113 (54.6%)	
Would improve your chances of having a lumpectomy (n=292)			0.21
Not important to somewhat important	62 (58.2%)	147 (54.1%)	
Important or very important	41 (41.8%)	75 (45.9%)	
Would make sure the cancer was removed by surgery as soon as possible (n=303)			0.002
Not important to somewhat important	34 (37.4%)	42 (19.8%)	
Important or very important	57 (62.6%)	170 (80.2%)	

See text for references for survey instruments. Total n was 331 if not shown

<sup>a</sup>Results are shown for analyses where those whose response was missing were excluded. Results were similar when a “missing” category was included

although this difference was not statistically significant ( $p=0.21$ ).

Also shown in Table 3 are patient reports of chemotherapy decision-making for the sample overall and by timing of chemotherapy. Subjects who received neoadjuvant chemotherapy were slightly more likely to report that they desired a more passive role in decision-making about their treatments (either the doctor makes the decision and considers my opinion or the doctor makes the decision with little input from me), but this difference was not statistically significant ( $p=0.22$ ). The difference was larger, though still not statistically significant, when subjects were asked about the role in the decision they *actually* played, with 34% of patients who received neoadjuvant chemotherapy having a more passive decision-making role as compared with 24% of those who received adjuvant chemotherapy ( $p=0.06$ ). There were no differences by timing of chemotherapy in response to a similar item asking about the actual role of family participation.

Subjects who received neoadjuvant chemotherapy reported similar quality of communication regarding cancer

treatment compared with those receiving adjuvant chemotherapy. They also reported similar quality of coordination of care overall, and in response to each of the individual items that made up the coordination score.

### Potential mechanisms for variation in chemotherapy timing by income

Given the differences in subjects' ratings of the importance of neoadjuvant advantages/disadvantages by timing of chemotherapy, we explored their potential role in the variation of chemotherapy timing by income. In all three cases, high-income subjects were less likely to consider the advantage/disadvantage as important. Specifically, 54.8% of high-income subjects reported that treatment that “allowed you to know the cancer had shrunk” was important or very important compared to 67.8% of lower-income subjects ( $p=0.04$ ), 19.7% of high-income subjects reported that “improving your chances of a lumpectomy” was important or very important compared with 46.9% of lower-income subjects ( $p<0.001$ ), and 60.3%

of high-income subjects reported that “making sure the tumor was removed by surgery as soon as possible” was important vs 79% for lower-income subjects ( $p = 0.005$ ). Only the result for “removed by surgery” would be consistent with a preference for neoadjuvant chemotherapy among higher-income patients (that is, higher-income patients were less likely to report that a benefit of adjuvant chemotherapy is important/very important). As would be expected given these differences by income, in models that adjusted for the responses “improving your chances of a lumpectomy” and “making sure the tumor was removed by surgery as soon as possible” the difference in neoadjuvant receipt between higher-income and lower-income subjects was actually widened (Table 4 in Appendix). In the model that included the subjects’ rating of importance of having the cancer “removed by surgery as soon as possible,” the differences in neoadjuvant use by income shown in Table 2 were narrowed but not fully explained (Table 4 in Appendix).

## Discussion

In this large, multicenter sample of women with invasive breast cancer, over 29% of patients who received chemotherapy received it before surgery. Receipt of neoadjuvant chemotherapy varied as expected by stage and cancer biomarker status, but women were also more likely to get neoadjuvant chemotherapy if they were older or in the highest SES groups (household income > \$100,000). Patients who received neoadjuvant chemotherapy rated the importance of its advantages higher, and the importance of its disadvantages lower, than those who received adjuvant chemotherapy. Although there were some differences regarding perceptions of the importance of benefits of neoadjuvant chemotherapy by income, these did not appear to be major factors in the association of income with chemotherapy timing. Patients’ reports of decision-making and quality of care were similar by timing of chemotherapy.

Our study findings regarding differences in treatment by income appears to conflict with one earlier report regarding neoadjuvant chemotherapy [1]. This study in the National Cancer Database found a lower likelihood of neoadjuvant chemotherapy with nonmetropolitan residence and older age, but residents of higher-income zip codes in that study were actually slightly—but not statistically significantly—more likely to receive neoadjuvant chemotherapy [1]. Our study used individual-level measures of income that were not available in the National Cancer Database, but it is not known whether that might explain the discrepancies in our findings. It is also notable also that our study is consistent with other studies

showing that lower-SES patients appear to be at higher risk of slow adoption of other advances in chemotherapy treatment, in some studies either not receiving chemotherapy despite indications for it [20] or being underdosed [21, 22].

We also were able to measure novel and detailed information about patient beliefs and preferences regarding neoadjuvant chemotherapy in our sample. Many patients valued the advantages of both neoadjuvant and adjuvant chemotherapy, but the relative importance of these advantages (and disadvantages) differed with the chemotherapy received. That these preferences also differed by income is concerning, though perhaps not that surprising given that information about neoadjuvant chemotherapy is probably new to many patients [23, 24]. Nonetheless, differences in preference by income did not appear to explain differences in chemotherapy timing by income; in fact, when perceived importance of the two neoadjuvant advantages was accounted for, differences by income increased. Future research that measures variation in preferences regarding neoadjuvant care prospectively, and with careful attention to health literacy and the information provided to patients, is needed.

There were no statistically significant differences by timing of chemotherapy in reports of desired or actual decision-making in our sample, although an association of more passive decision-making role with receipt of neoadjuvant chemotherapy was suggested ( $p = 0.06$ ). A more passive decision-making experience may be expected for a procedure that many patients are not aware of until it is actually offered to them. Many patients want an active role in breast cancer decision-making [14] so these findings should be examined in other settings and larger samples. Our results also showed similar patient-reported quality of communication and coordination by timing of chemotherapy. This is reassuring, given that the treatment experiences might be expected to be quite different, particularly since patients who had neoadjuvant chemotherapy had higher-stage disease that generally requires more complex treatment.

Our study has some limitations. Our reports of timing of chemotherapy were based on self-report, and it is possible some patients were unsure or mistaken in their reports. However, there is high validity to patient reports of chemotherapy receipt generally [11], and recall of its timing relative to surgery might be expected to be high 1–2 years after the experience as well. Our study was cross-sectional. It is possible that a prospective observation of counseling sessions (e.g., by use of audiotapes) would have had different findings about perceived advantages and disadvantages of neoadjuvant therapy. Our examination of specific measures of SES were somewhat limited by power, so that our ability to tease out differences between low income and low education was limited. There is evidence that a growing number of patients

do not need cytotoxic chemotherapy [25–27], and it is possible that factors associated with timing of chemotherapy will change as the cohort of patients receiving chemotherapy shrinks. Finally, our results may be affected by survival bias or selection bias if patients with shorter survival or who did not participate in the study would have reported a different relation between chemotherapy timing and experiences than women who did participate. However, early mortality is low in breast cancer [28] even among patients with stage 2 and 3 disease.

Despite these limitations, our study provides important information regarding patients' preferences and experiences with neoadjuvant chemotherapy compared with adjuvant chemotherapy. Our study's findings regarding large differences in use of neoadjuvant chemotherapy by income have important implications. While these results are consistent with the patterns seen for adoption of other new technologies and therapies, it is particularly important in breast cancer given the restriction of many new breast cancer trials to neoadjuvant users. Variability in neoadjuvant use by income could perpetuate or even worsen disparities in clinical trial enrollment, and deserves further research and if confirmed, urgent attention.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Research involving human participants** All procedures performed in studies involving human participants were in accordance with the ethical standards of the University of Iowa institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all participants included in the study.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Appendix

See Table 4.

**Table 4** The association of income with neoadjuvant chemotherapy use, with adjustment for importance to patients of the advantages/disadvantages of neoadjuvant chemotherapy

	Primary model (n=303)	Model with Patient-reported Importance Variable (n=303)	Primary model (n=292)	Model with Patient-reported Importance Variable (n=292)	Primary model (n=303)	Model with Patient- reported Importance Variable (n=303)
	Adjusted OR (CI 95%)	Adjusted OR (CI 95%)	Adjusted OR (CI 95%)	Adjusted OR (CI 95%)	Adjusted OR (CI 95%)	Adjusted OR (CI 95%)
<b>Income</b>						
Greater than \$100,000 (reference)	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
Less than \$100,000	0.55 (0.29, 1.04)	0.36 (0.17, 0.76)	0.57 (0.30, 1.08)	0.45 (0.23, 0.88)	0.51 (0.27, 0.96)	0.58 (0.31, 1.1)
Missing income	1.47 (0.57, 3.78)	0.86 (0.28, 2.35)	1.45 (0.56, 3.81)	1.18 (0.43, 3.16)	1.21 (0.46, 3.20)	1.48 (0.54, 4.03)
<b>Cancer Shrunk</b>						
Not important to somewhat important	-	0.08 (0.04, 0.20)				
Important or very important	-	(reference)				
<b>Chances Lumpectomy</b>						
Not important to somewhat important			-	0.43 (0.23, 0.80)	-	-
Important or very important			-	(reference)	-	-
<b>Removed by Surgery</b>						
Not important to somewhat important					-	2.14 (1.14, 4.01)
Important or very important					-	(reference)

Because those with missing data for these variables were excluded from the models, results for income vary slightly from Table 1. The models were also adjusted for age, stage, and cancer subtype as in Table 1. Analyses done with missing categories for all variables were similar

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