Timeliness and acceptance of recommended treatment in newly diagnosed breast cancer patients

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Abstract

Breast cancer is the most common cancer in women and it is the second leading cause of cancer-related death in women in the United States. Although evidence-based recommendations for breast cancer care are well established, scant literature has documented patients' acceptance of recommended treatments. Disease and non-disease factors associated with non-acceptance remain unclear. Non-acceptance of recommended treatments can result in delayed initiation of effective treatment and failure to complete planned treatment. Both are known to be associated with a higher recurrence rate and may be reasons for disparities in breast cancer related survival. This study aimed to develop a metric to evaluate timeliness and patients' acceptance of recommended treatment in newly diagnosed breast cancer patients and to identify factors associated with meeting the quality benchmarks and patients' acceptance of the treatment.

We reviewed 247 newly diagnosed breast cancer patients presented to Tufts Medical Center between January 2009 and June 2013. Of the patients who had surgery recommended as the first treatment, 80% (176/219) met the 45-day time-to-surgery benchmark with a median of 28 days to surgery. Of the patients who were stage I-III hormone receptor-positive, 92% (138/150) met the 365-day hormone therapy benchmark with a median of 145 days to hormone therapy. Analysis of acceptance by a single modality showed that 74% (17/23) of patients accepted neoadjuvant chemotherapy, 97% (232/240) accepted surgery, 83% (130/157) accepted radiation, 71% (85/119) accepted adjuvant chemotherapy, and 85% (155/183) accepted hormonal therapy. Overall, among 238 patients with known initiation of treatment, 61% accepted all recommended treatments, 21% rejected at least one treatment, and 18% had

incomplete information. Multivariable regression showed that after adjusting for insurance, family history of breast cancer, prior history of breast cancer treatment, and comorbidity, older age (OR, 95%CI: 1.30, 1.12-1.53) and higher median household income by census tract (OR, 95%CI: 1.11, 1.03-1.19) were associated with meeting the 45-day time-to-surgery benchmark. These findings may help us identify patient populations at increased risk of delaying and/or not accepting recommended treatments and to inform the development of interventions and policies that are aimed toward improving timely and quality of breast cancer care.

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List of Abbreviations

AACR	American Association for Cancer Research
AJCC	American Joint Committee on Cancer
CHT	Chemotherapy
CI	Confidence interval
DCIS	Ductal Carcinoma in Situ
EMR	Electronic Medical Record
ER	Estrogen receptor
HER2	Human epidermal growth factor receptor 2
HT	Hormone therapy
IQR	Interquartile range
MiBOQI	Michigan Breast Oncology Quality Initiative (MiBOQI)
MC	Medical Center
NCCN	National Comprehensive Cancer Network
NACT	Neoadjuvant chemotherapy
NQF	National Quality Forum
PR	Progesterone receptor
REDCap	Research Electronic Data Capture
RT	Radiation therapy

1. Introduction

1.1 Breast Cancer Incidence and Trends

According to World Health Organization (WHO), breast cancer has the highest global prevalence and is the most common cancer in women worldwide (Global Health Estimates, WHO 2013). In 2015, an estimated 13% of all new cancer cases and 26% of all cancers in women are breast cancer (Cancer Facts & Figures, American Cancer Society, 2015-2016). According to the World Cancer Research Fund International, both the worldwide incidence of breast cancer and mortality from it have increased (20% and 14%, respectively) since 2008 (Ferlay et al., 2012).

In the United States (US), breast cancer is also the most commonly cancer in women and the second leading cause of cancer death among women. According to National Breast Cancer Facts and Figures 2015, 1 in 8 women in the U.S. will be diagnosed with breast cancer in her lifetime. It is estimated that each year about 250,000 women in the US will be diagnosed with breast cancer and more than 40,000 will die of breast cancer. Although breast cancer has the highest incidence of all cancers affecting U.S. women, recent years breast cancer incidence rates have declined among women aged 50 and older, in part due to the decline in prescriptive hormone replacement therapy after menopause. Mortality from breast cancer also has been declining since 1990, attributable to better screening technology and early detection, increased awareness and education, and continually improved treatment regimens. According to the 2015 Cancer Facts & Figures from the American Cancer Society, the 5-year relative survival rate for female invasive breast cancer has improved from 75% in the mid-1970s to 90% in 2015, and the 5-year relative survival rate for localized breast cancer (cancer has not spread to lymph nodes or outside the breast) is 98.5%. The survival rates of breast

cancers that have spread to nearby lymph nodes and to distant lymph nodes and organs remain lower at 84% and 24%, respectively.

1.2 Breast Cancer Health Disparities

Although breast cancer survival rates generally have improved overall, not all patients benefit equally from timely screenings and advances in treatment regimens. Differences in clinical outcome of breast cancer have been documented. The breast cancer incidence among Black women (117 in 100,000) is lower than that among White women (122 in 100,000), however, the breast cancer mortality rate is higher among Black women (National Breast Cancer Facts and Figures 2015). A recent study using a cohort from 2005 to 2008 in Center for Medicare and Medicaid Services (CMS) claims data revealed that Black women had a mean of 15.7 more days from screening mammogram to treatment and 16.7 more days from biopsy to treatment than White women (Selove et al, 2016). In this CMS cohort, the median duration from abnormal mammogram to treatment initiation is over 43 days, which exceeded the National Quality Measures for Breast Center median value of 28 days, regardless of race, age, or number of comorbidities.

Multiple studies have documented factors that are associated with breast cancer disparities, including differences by socioeconomic and race/ethnic groups. Specifically, these studies have shown that uninsured women or those insured through Medicaid in general present with a more advanced stage of disease than those with private insurance (Bradley et al., 2002). Lower socioeconomic groups have been shown to be less likely to have timely care after abnormal screening mammography (Battaglia et al., 2011; Ko et al., 2014). They also experience delays in treatment (Bleicher et al., 2012;

Gagliato Dde et al., 2014) after diagnosis, fail to opt for the most efficacious treatment regimens, and be less likely to adhere to recommended treatment (Bickell et al., 2007). Minority race/ethnicity and lower socioeconomic status, as measured by low family income, poor educational attainment, and limited access to health care insurance, have all been shown to be associated with longer intervals between diagnosis and treatment initiation (McLaughlin et al., 2012) and longer time to adjuvant chemotherapy (Bleicher et al., 2012; Chavez-MacGregor et al., 2016; Vandergrift et al., 2013).

Excessive delays in treatment may be one component of why disadvantaged groups experience worse breast cancer outcomes (Brawley, 2013). A British Columbia cohort study reported that time to chemotherapy of longer than 12 weeks after surgery was associated with significantly worse overall survival (Lohrisch et al., 2006). Another prospective study evaluated time to surgery using two large and independent national datasets revealed that every 30-day increment in pre-operational interval was significantly associated with a decline in overall survival rate in stage I and II breast cancer patients (Bleicher et al., 2016). These studies suggest that effects to expedite breast cancer care have great clinical value given breast cancer survival is a function of time from diagnosis to treatment. Understanding what specific factors at patient, clinician, and health care system level may lead to breast cancer disparities is crucial to inform the implementation of thoughtful interventions to expedite the initiation of treatment.

1.3 Quality Benchmarks for Timeliness of Breast Cancer Care

Many efforts have been made to eliminate breast cancer healthcare disparities. For example, Centers for Disease Control and Prevention (CDC) has administered The

National Breast and Cervical Cancer Early Detection Program since 1990 to provide medically underserved women with access to timely breast and cervical cancer screening and diagnostics services. Patient navigations programs also have been used to address patients' barriers to timely breast cancer care. Despite improved access to breast cancer screening, the median interval from breast cancer diagnosis to surgery in Medicare patients with breast cancer increased from 21 days in 1992 to 32 days in 2005 (Bleicher et al., 2012) and the median time interval from diagnosis to adjuvant chemotherapy of patients from nine National Comprehensive Cancer Network (NCCN) centers increased from 76 days in 2003 to 93 days in 2009 (Vandergrift et al., 2013). Delays in effective treatments are known to be associated with poor clinical outcomes, and moreover, the delays are lengthening over time. Thus the effects of delaying treatment have been becoming an increasingly important consideration (McLaughlin et al., 2012). Currently, several disease-specific consortia and government agencies, such as the National Quality Forum (NQF), CDC, and Michigan Breast Oncology Quality Initiative (MiBOQI), have developed quality benchmarks or standards related to breast cancer care. These benchmarks and standards serve as a critically important foundation for initiatives to enhance healthcare values, make patient care safer, and achieve better outcomes.

Timeliness benchmarks of breast cancer care from NQF

One widely cited set of measures is from NQF, a consensus standards-setting organization with a mission to improve the quality of American health care. Quality measures, established by NQF, are endorsed by the American Society of Clinical Oncology and the NCCN for breast cancer. NQF quality measures reflect evidence from randomized controlled trials that evaluated survival benefits for patients receiving adjuvant radiation, chemotherapy, and hormone therapy (Early Breast Cancer Trialists'

Collaborative, 2005; Fisher et al., 2002; Veronesi et al., 2002) Currently, NQF has established six quality measures related to breast cancer treatment and four of them relate to timeliness of care for clinical defined patient subgroups (**Table 1.1**).

Table 1.1 National Quality Forum timeliness quality benchmarks

Quality Measure	Patient subgroup	Time-defined benchmark
Initiation of adjuvant hormone treatment	- Age >18 - AJCC stage T1cN0M0 or IB to III breast cancer - Primary tumor progesterone receptor (PR) and/or estrogen receptor (ER) +	Tamoxifen or aromatase inhibitor within **1 year** of diagnosis
Adjuvant combination chemotherapy	- Age 18-69 - AJCC T1cN0M0, or Stage IB - III (tumor greater than 1 cm) - ER and PR -	Multiagent chemotherapy Within **120 days** of diagnosis
Hormonal therapy	- Age > 18 - Stage IC to IIIC - ER and/or PR +	Tamoxifen or aromatase inhibitor (AI) within **1 year** of diagnosis
Post breast conservation surgery irradiation	- Age 18-69 - AJCC stage I, II, or III breast cancer - Received breast conserving surgery	Radiation therapy within **1 year** of diagnosis

These NQF measures have been used to assess quality of breast cancer care and compliance with these measures in various health care setting and in minority and/or underserved patient population. In a recent study, Castaldi et al. reported poor compliance with the 365-day initiation of hormone therapy, 120-day initiation of chemotherapy, and the 365-day post-surgery radiation benchmarks at six public safety net hospitals. The study found that implementation of a multidisciplinary patient navigation program reduced time to treatment and improved compliance with adjuvant therapy for breast cancer in an underserved minority community (Castaldi et al., 2016).

Michigan Breast Oncology Quality Initiative (MiBOQI)

In 2006, the University of Michigan Comprehensive Cancer Center, in collaboration with the NCCN and Blue Cross Blue Shield of Michigan, established the MiBOQI with a mission to improve the treatment and outcomes of breast cancer. It collects network-based demographic, diagnostic, treatment, and outcome data to inform evaluation of current standards of care and to initiate quality improvement efforts that will advance breast cancer treatments in order to improve patient outcomes. Since then, MiBOQI has established a timeliness benchmark for surgery in which if surgery is recommended as the first treatment, it should be initiated within 45 days after biopsy (Breslin et al., 2011; Smith et al., 2011). This benchmark is currently used for reporting to American College of Surgeons' Commission on Cancer.

The 60-day benchmark from CDC

Since 1990, CDC has administered The National Breast and Cervical Cancer Early Detection Program to provide medically underserved women with access to timely breast and cervical cancer screening and diagnostics services. Since the inception of the program, it has developed service delivery benchmarks to ensure timely and complete diagnostic follow-up and treatment initiation for underserved women screened through the program. The 60-day benchmark of breast cancer treatment initiation was one of the first benchmarks developed in the studies that explored the time required to begin treatment through The National Breast and Cervical Cancer Early Detection Program (Caplan et al., 2000, Richardson et al in 2010). This benchmark measures whether breast cancer patients initiate *any* recommended treatments within 60 days of diagnosis. It has been widely used to assess or report timeliness of quality of breast cancer care.

1.4 Patients' Acceptance of Recommend Treatment

Evidence-based guidelines for breast cancer treatment have been well-established for subgroups of patients by tumor stage, hormone receptor status, menopause status, comorbidity, prior treatment history, genetic mutations, and family history (NCCN guidelines). The treatment regimens may combine neoadjuvant chemotherapy, surgery, adjuvant chemotherapy, radiation, and hormone therapy. In some cases, patients may be offered multiple treatment options that are equally effective. The use of multiple modalities in the treatment of breast cancer can complicate patients' acceptance of the treatment plans, as they interact with multiple specialists and consider the risks and benefits of each modality. Moreover, as the treatment regimen can last up to 5 years or longer, concerns about long-term impacts of side effects from radiation, chemotherapy, and hormone therapy (Body et al., 2016; Overbeek et al., 2016) on social and personal relationships also influence patients' acceptance of recommended treatments. Moreover, non-disease related factors, such as socioeconomic status, culture factors, education factors, race/ethnicity factors, and language factors, can influence patients' acceptance of recommended treatment. Therefore, patients' acceptance of all recommended treatments is a dynamic and multifactorial process that involves participation of patients, patients' families or social support network, health care providers, and other health professionals such as health insurance plan. For all these reasons, some patients do not accept all recommended modalities and some even do not initiate treatment.

Non-acceptance of recommended treatments can result in delayed initiation of effective treatment and failure to complete treatment plan. Both are known to be associated with a higher recurrence rate and may be reasons for disparities in breast cancer-related survival. Although assessment of patients' acceptance of recommended treatments is important for quality measures of breast cancer care, limited research has been performed on the assessment of patients' acceptance due to difficulty in documenting timeliness and completeness of all modalities that patients have received

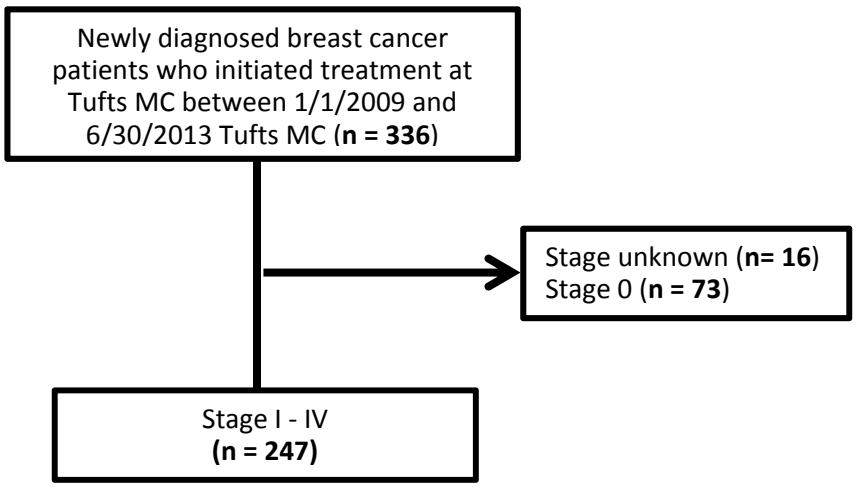
and difficulty in comparing them with all recommended modalities. Therefore, the goal of this study was to characterize both the timeliness of breast cancer care, using national benchmarks, as well as to evaluate patients' acceptance of recommended treatment across modalities. The study also sought to identify factors that are associated with meeting the timeliness benchmark and all-acceptance of the treatment plan.

2. Materials and Methods

2.1 Study population

This retrospective study included newly diagnosed breast cancer patients presented at Tufts Medical Center (MC) between January 1, 2009 and June 30, 2013. We initially identified 336 newly diagnosed breast cancer patients from Tufts MC Tumor Registry and Tufts Cancer Center patient navigation screening database. After excluding 73 patients with stage 0 and 16 patients with unknown stage, a total of 247 stage I - IV breast cancer primary patients were included in the statistical analysis (**Figure 2.1**). The study was approved by the Tufts MC Institutional Review Board.

Figure 2.1 Study population



2.2 Data collection

Data sources

For an initial screening, a list of all newly diagnosed breast cancer patients with their name, the date of diagnosis, and the Medical Record Number (MRN) were obtained. Using the unique MRN, patient demographics and disease characteristics were retrieved from two data sources: the electronic health record, known as MOSAIQ, used in the Tufts Cancer Center and administrative data, stored in Soarian. The MRN was linked to a unique study ID for data abstraction. The date of the last biopsy that led to a definitive diagnosis of cancer was abstracted and recorded as the diagnosis date (Time 0). Clinical notes of patients were followed for up to one year from the diagnosis date. One-month windows prior to Time 0 and beyond one year follow-up were allowed to assure completeness of data abstraction.

Development of abstraction protocol and data abstraction

All data were collected using a pre-designed abstraction form (**Appendix Abstraction Form**). The abstraction form and the data collection protocol were finalized and evaluated through a pilot data collection and group training. Dual data abstraction was conducted for each case and discrepancies between two abstractors were reconciled with study oncologists. To ensure data quality, the collaborating oncologists completed all grading of co-morbidities after an initial 10% review of the reconciled data revealed bidirectional errors (over- and under-attribution). All data were entered into a web-based clinical data management platform Research Electronic Data Capture (REDCap). The dataset was de-identified with respect to patient name and MRN, but did contain dates of service in order to calculate the timeliness outcomes.

2.3 Variables

Demographics including date of birth, sex, race/ethnicity (White, Black/African-American, All others), language (English, non-English), marital status (currently

married/partnered and single/widowed/divorced/separated), address, and health insurance coverage at the time of diagnosis were obtained from administrative information in Soarian. Age at diagnosis was calculated using the date of birth and the date of diagnosis. The median household income by census tract was obtained from the US Census Bureau's American Fact Finder (factfinder.census.gov/) using the street address. Family support was defined if any medical note documented at least one presence of a family member at a clinical visit during one year follow-up time. Names of insurance plan were obtained from administrative database and then categorized into: "Private only", "Any subsidized plan" (including any Medicare, MassHealth, and/or any exchange product), and "No insurance".

Disease characteristics including the date of diagnosis, tumor stage, hormone receptor positivity, family history of breast cancer, prior history of breast cancer treatment, and comorbidity at the time of diagnosis were abstracted from medical notes. 'Multiple biopsies' was defined if a patient had received more than one biopsy prior to the final determination of the cancer diagnosis. Tumor stage was recorded in anatomic stages (0- IV) using AJCC breast cancer staging systems. Pathological positivity of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) were recorded. Hormone receptor positivity was dichotomized as "any ER and/or PR positive" or "No". Triple negative breast cancer was defined as "Yes" if ER, PR and HER2 were all negative. Family history of breast cancer was defined as "Yes" if any first and/or second degree relatives of a patient had a prior breast cancer diagnosis. Prior history of breast cancer treatment and the presence of comorbid conditions were abstracted from patients' medical history notes. Patients' comorbidity at the time of diagnosis was abstracted by recording the presence of any of 22 clinical conditions listed in **appendix Table 5.1** (Charlson et al., 1987; Deyo et al., 1992, and

Quan et al., 2005). The Charlson comorbidity score of each patient was calculated by study oncologists using the established scoring system. For the statistical analysis, the comorbidity status was dichotomized into: no comorbidity (score = 0) and has comorbidity (score = 1 - 8).

2.4 Primary outcome

The primary outcome is patients' acceptance of recommended treatment which has two components: timeliness of care and acceptance of treatment plan across modalities. To assess timeliness of care, we evaluated two quality benchmarks given the frequency of these treatment recommendations within the study population: 1) receipt of surgery within 45 days of diagnosis in patients with surgery recommended as the first modality and 2) initiation of hormone therapy within 365 days of diagnosis in stage I-III hormone receptor positive breast cancer patients. Evaluable cases for each benchmark were first identified and the proportion of patients who met the benchmark in each scenario was presented. We explored additional benchmarks for less frequently recommended modalities in our study population (see supplemental materials). To ascertain reasons of delay in extreme cases, we reviewed the individuals with the top decile of surgery delay (not meeting the 45-day time-to-surgery benchmark) and all cases with hormone therapy delay (not meeting the 365-day benchmark).

Recommended treatments and treatments patient received were abstracted from medical notes. Whether each of the following modalities, including neoadjuvant chemotherapy, surgery, radiation, adjuvant chemotherapy, and/or hormone therapy, was recommended was recorded as "Yes", "No", or "Not stated". Whether a patient received the recommended treatment was abstracted as "Yes", "No", or "Unknown". If a patient received the recommended treatment, the dates of the start and the completion of the treatment were recorded. A lost to follow-up case was defined if a patient stopped

seeking breast cancer care at Tufts MC before the completion of all recommended treatments within one year period following diagnosis. For all lost to follow-up patients, the date of the last clinical visit was recorded and the patient was censored at the date of last visit for Kaplan-Meier estimation.

Acceptance by a single modality was defined based on the outcome combining whether the modality was recommended and whether the patient received it (as described in **Table 2.1**). The outcome by a single modality included: accepted, probably accepted, not accepted, not applicable, and incomplete information. The category 'probably accepted' was used in those cases in which the specific treatment recommendation was not found, but the patient received the modality. We assumed that patients would not receive a treatment without physician recommendation.

Overall acceptance of each patient was determined based on a combination of all modality outcomes. Overall acceptance had three categories (**Table 2.2**): 1) not all accepted, defined as a patient rejected any one or more recommended modalities; 2) all accepted, defined as a patient received all recommended treatments except those were not recommended; and 3) incomplete case, defined as a patient had any incomplete information in any treatment modality.

Table 2.1 Definition of acceptance by a single modality.

Recommendation	Whether patient received		
	No	**Yes**	**Unknown**
No	Not applicable	Not applicable	Not applicable
Yes	Not accepted	Accepted	Incomplete info
Not stated	Incomplete info	Probably accepted	Incomplete info

Table 2.2 Definition of acceptance of overall modalities.

Overall acceptance	Combination of acceptance by modality
1) Not all accepted	Any modality that had "Not accepted"
2) All accepted	Modality that had "Accepted", "Probably accepted", and/or "Not applicable"
3) Incomplete case	Any modality had "Incomplete information"

2.5 Missing data

Missingness of demographic variables was summarized in **Appendix Table 5.2s**. No variable had missingness exceeded a pre-set threshold 10%, therefore, all demographic variables were included in statistical analysis. Patients with stage unknown (n=16) was not included in the main analysis and was summarized in supplemental materials to assess risk of bias. For patients' overall acceptance, any case with a missing value in modality recommendation or acceptance is considered as an incomplete case. Comparisons between complete cases and incomplete cases in their demographic were conducted (see supplemental materials) to assess risk of bias. Missingness of outcomes was summarized in **Appendix Table 5.2b**.

2.6 Data analysis

Descriptive analysis

Patient and disease characteristics for the study population were summarized in descriptive statistics. Continuous variable age was presented in mean (SD) and median household income in median (25^{th} and 75^{th} percentiles). Binary outcomes including language, insurance, marital status, family support, triple negative, hormone receptor positivity, family history, prior breast cancer treatment history, and comorbidity, and categorical variables including race and tumor stage were presented in N (%).

For descriptive statistics of groups by stage known vs stage unknown and complete cases vs non-complete cases, a student t-test was used to compare means of age, a Mann-Whitney test was used to compare medians of household income by census tract, and a Chi-squared test or a Fisher exact test were used for all other categorical variables. $p<0.05$ is indicated in bold.

For the timeliness benchmarks, N (%) of evaluable cases meeting/not meeting the 45-day time-to-surgery benchmark and the 365-day hormone therapy benchmarks were

reported. Time to surgery and hormone therapy initiation was presented in Kaplan-Meier curve and the median day (25^{th} and 75^{th} percentiles) to the treatment initiation was reported. To explore the reasons of delays, we reviewed the top decile of delays in reaching the 45-day surgery benchmark and all delays in the 365-day hormone therapy benchmark. Individual time to treatment initiation and and the documented reasons for the delay were listed. We then conducted thematic analysis to summarize reasons. The number (%) of meeting/not meeting other timeliness benchmarks (60-day treatment initiation, 120-day chemotherapy, and 365-day post-surgery radiation), median days (25^{th} and 75^{th} percentiles) to treatments, and descriptive analysis for the group comparison between meeting/not meeting 60-day benchmark are presented in supplemental materials.

Patients' acceptance of recommended treatment was analyzed at two levels: acceptance by a single modality and overall acceptance. N (%) of "Accepted", "Not accepted", and "Incomplete cases" by a single modality and N (%) of "All accepted", "Not all accepted", and "Incomplete cases" of overall acceptance were reported. Patient and disease characteristics for two-group comparison between "All accepted" versus "Not all accepted" were summarized in descriptive statistics.

Univariable analysis and multivariable logistic regression

Univariable analysis and multivariable logistic regression were conducted to identify factor(s) associated with meeting the 45-day time-to-surgery benchmark. Similar analyses were also conducted for the 60-day benchmark and the all-acceptance outcome (in supplemental materials). For multivariable logistic regression, the following variables were included in the model regardless of univariable screening: age, insurance, family history of breast cancer, prior treatment history of breast cancer, and

comorbidity. Variables with a p-value less than 0.2 from univariable screening were added to the multivariable regression model. The model was diagnosed using c-statistics and the area under the curve (AUC) was reported. Linearity assumption for continuous variables was assessed. Influential observations were assessed using Pearson residual and deviance residual and no outlier was excluded from the analysis. Linearity assumption was assessed for continuous variables by plotting fitted value against data value with a straight line of lowess curve indicating a linear relationship. P-value was two-sided throughout and statistical significance was set at P = .05. All statistical analyses were performed using R.

3. Results

3.1 Patient characteristics

Patient characteristics are summarized in **Table 3.1**. The majority of patients (67%) were White, 13% were Black/African-American, and 20% were all others which included 2% Hispanic/Latino, 13% Chinese origin, and 5% other Asian. The majority of patients (84%) were English-speakers and 16% were non-English speakers which included 3% Mandarin speakers, 10% Cantonese speakers, and 3% other Chinese speakers. 41% of patients had only private insurance and 57% had subsidized insurance, which included 30% Medicare, 15% MassHealth, 11% dual Medicare and MassHealth, and 1% other exchange products. The distribution of Charlson comorbidity scores is displayed in **Appendix Figure 5.1**.

Table 3.1 Patient characteristics

Patient characteristic	N=247
Mean age, y(SD)	60 (14)
Race/ethnicity	
White	164 (67%)
Black/African-American	33 (13%)
All others	49 (20%)
Language	
English	208 (84%)
Non-English	39 (16%)
Census tract median household income, median (25^{th}, 75^{th} percentiles)	$71,450 ($56,120 - $90,410)
Insurance	
Private only	100 (41%)
Any subsidized*	140 (57%)
Marital status	
Currently married/partnered	142 (57%)
Single/Widowed/divorced/separated	105 (43%)
Family support	
Yes	139 (56%)
No	108 (44%)
Tumor stage	
Stage I	151 (61%)
Stage II	60 (24%)
Stage III	25 (10%)
Stage IV	11 (4%)
Triple negative	
Yes	32 (13%)
No	214 (87%)
Hormone receptor positivity	
ER and/or PR positive	208 (84%)
No	38 (15%)
Multiple biopsy (Yes)	
Yes	36 (15%)
No	211 (85%)
Family history of breast cancer	
Yes	112 (45%)
No	131 (53%)
Prior history of breast cancer treatment	
Yes	22 (9%)
No	224 (91%)
Comorbidity	
Charlson score 0	156 (63%)
Charlson score 1-8	90 (37%)

*"Any subsidized" included "Medicare only", "MassHealth only", "Medicare and MassHealth" and "Any other exchange product". Data are shown as mean ± SD or median (25th, 75th percentiles) or N (%).

3.2 Quality benchmarks for timeliness of breast cancer care

Among 219 (89%) patients with surgery recommended as the first treatment, 80% (176/219) met the 45-day time-to-surgery benchmark. Among 150 (61%) patients with stage I - III tumor who also were hormone receptor-positive, 92% (138/150) met the 365-day hormone therapy benchmark (**Table 3.2**). Identification of evaluable cases for the hormone therapy benchmark is presented in appendix **Table 5.3**. The median intervals (25^{th} to 75^{th} percentiles) to surgery and to hormone therapy were 28 days (18 - 41) and 145 days (75 - 220), respectively (**Figure 3.1 and Figure 3.2**). Numbers and percentages of patients who met additional quality benchmarks (60-day initiation of treatment, 120-day initiation of adjuvant chemotherapy in stage I - III triple-negative patients, and 365-day initiation of radiation therapy in patients received breast-conserving surgery) and the median intervals between diagnosis and treatment are summarized in **appendix Table 5.4**.

Table 3.2 Quality benchmarks for surgery and hormone therapy

Treatment Benchmarks	**N (%)**
45-day benchmark when surgery was recommended as the first treatment (N=219)	
< = 45 days	176 (80)
> 45 days	43 (20)
Stage I-III hormone receptor-positive breast cancer with hormone therapy (N=150*)	
< = 365 days	138 (92)
> 365 days	7 (5)
Unknown#	5 (3)

*Identification of evaluable cases was presented in Appendix Table 5.3.
Unknown cases were not presented in KM curve in Figure 3.2

Case review of surgery delays identified 21 cases with the interval to surgery in excess of 57 days (range: 57-183), corresponding to the top decile. The individual time to surgery and reasons for delay of the top decile are presented in **Table 3.3**. For the hormone therapy benchmark, we reviewed all seven cases with delays ranged from 368

to 492 days and reasons for delays are presented in **Table 3.4**. Themes identified as reasons of the delays in receipt of initial surgery and hormone therapy included clinical complexity, insurance issues, seeking a second opinion, treatment indecision, missing appointments, or an unclear reason.

Table 3.3 Case review for reasons of the top decile surgery delays

Case	Time to Surgery (days)	Reasons of delay
1	183	Change of insurance
2*	181	Unclear
3	132	Multiple biopsies
4	99	Come to Tufts MC for a second opinion
5	95	Clinical complexity
6	92	Treatment indecision
7**	90	Missed appointments
8	82	Unclear
9	77	Insurance coverage
10	75	Unclear
11	73	Clinical complexity
12	67	Personal issue (travel)
13	66	Clinical complication/Unclear
14	66	Come to Tufts MC for a second opinion
15	63	Clinical complexity
16	62	Come to Tufts MC for a second opinion
17	62	Clinical complexity
18	61	Clinical complexity
19	61	Personal issue/Clinical complexity
20	60	Unclear/clinical complexity
21	57	Unclear

Table 3.4 Case review for reasons of delays in hormone therapy

Case	Time to hormone therapy (days)	Reasons of delay
1	492	Clinical complexity
2	454	Clinical complexity
3*	424	Unclear
4**	421	Missed appointments
5	420	Clinical complexity
6	385	Gap in medication coverage
7	368	Personal/Family issue

*The case No. 3 in Table 3.4 and the case No. 2 in Table 3.3 are the same patient.
** The case No.4 in Table 3.4 and the case No.7 in Table 3.3 are the same patient.

Figure 3.1 KM curve of the 45-day time-to-surgery benchmark.

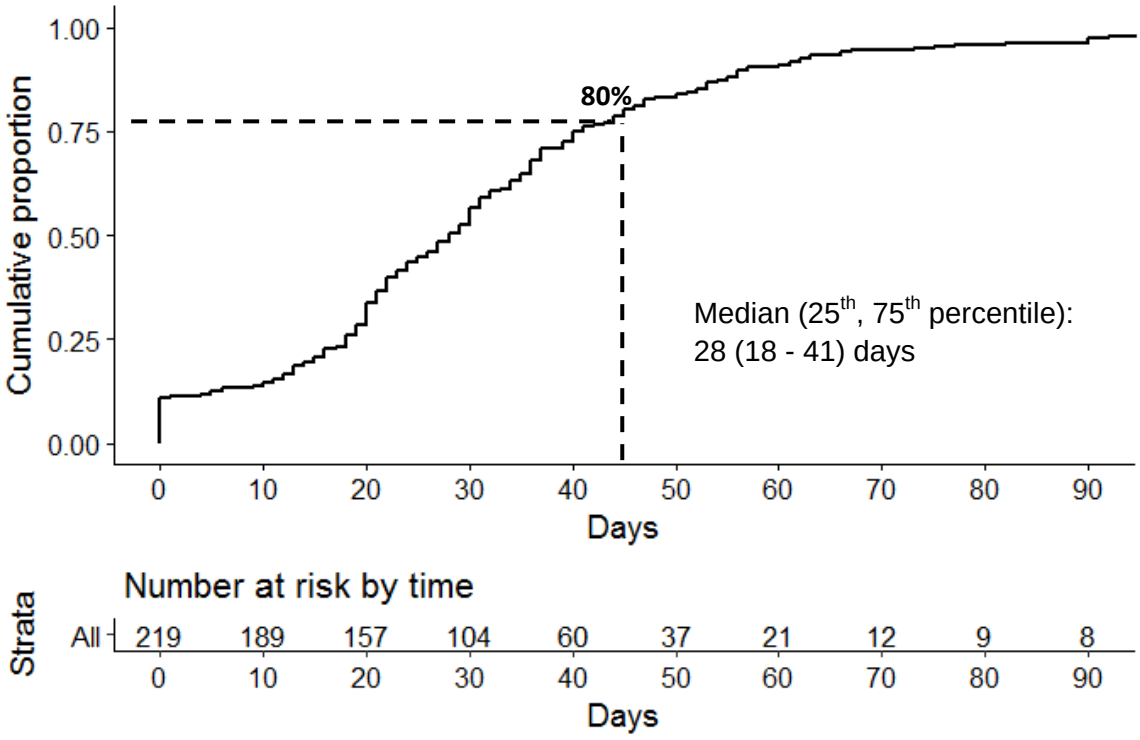
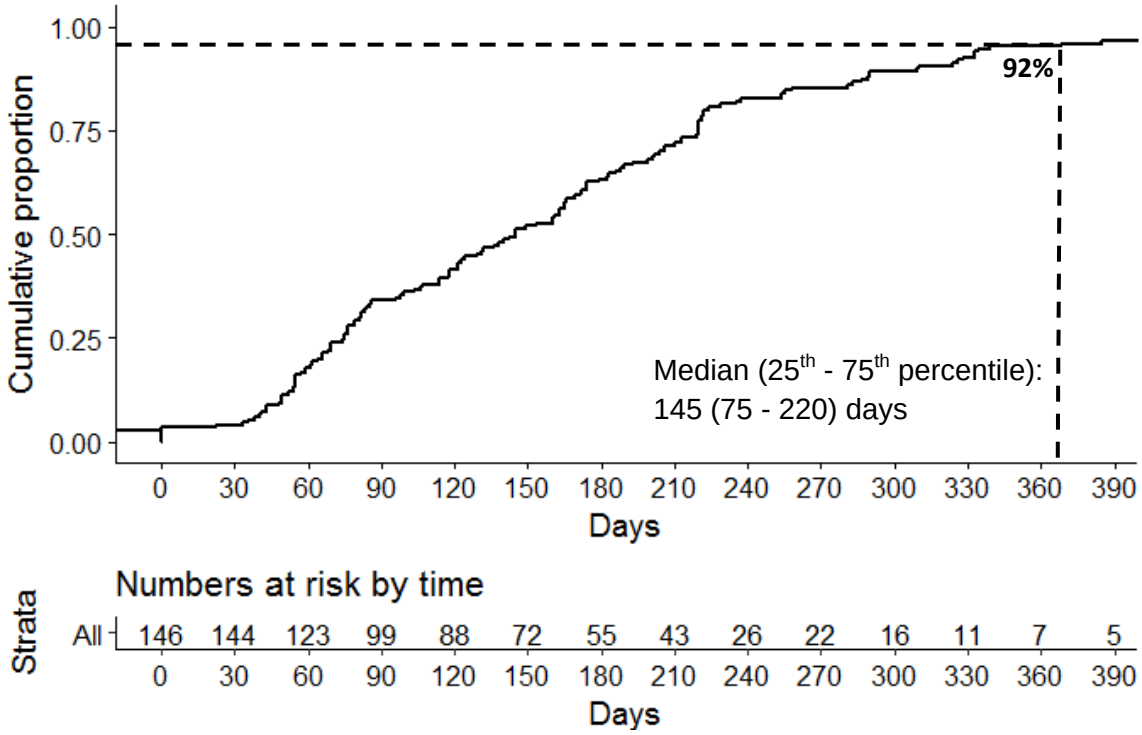


Figure 3.2 KM curve of 365-day hormone therapy benchmark.



Additionally, we evaluated three other established timeliness benchmarks: the 60-day benchmark of treatment initiation, 120-day benchmark for initiation of adjuvant chemotherapy, and the 365-day benchmark for initiation of radiation therapy (**Appendix Table 5.4**). The 60-day benchmark result showed that 89% (213/238) of patients met the benchmark (**Appendix Table 5.5 and Table 5.6**) with a median time to treatment initiation of 29 days (25^{th}-75^{th} percentiles: 18-41), which was similar to the results of the 45-day benchmark. Seventy-three percent (11/15) of patients with stage I-III with triple-negative breast cancer met the 120-day benchmark of adjuvant chemotherapy with a median time to treatment initiation of 84 days (25^{th}-75^{th} percentiles: 75-103). Ninety-two percent (100/109) of patients who had received breast-conserving surgery met the 365-day radiation benchmark and the median time to radiation treatment of was 132 days (25^{th}-75^{th} percentile: 70-201).

Characteristics of patients who met and did not meet the 45-day surgery benchmark are summarized in **Table 3.5**. Univariable analysis showed that older age and living in a community with higher median household income were significantly associated with meeting the 45-day time-to-surgery benchmark. After adjusting for age, insurance, family history of breast cancer, prior treatment history of breast cancer, and comorbidity, older age and higher median household income by census tract were significantly associated with meeting the 45-day time-to-surgery benchmark (**Table 3.6**).

Table 3.5 Patient characteristics by the 45-day time-to-surgery benchmark

Patient characteristic	Meeting benchmark <= 45 days (N = 176)	Not meeting benchmark >45 days (N = 43)
Mean age, y(sd)	62 (13)	56 (14)
Race/ethnicity		
White	121 (69%)	27 (63%)
Black/African-American	23 (13%)	6 (14%)
All others	31 (18%)	10 (23%)
Language		
English	148 (84%)	36 (84%)
Non-English	28 (16%)	7 (16%)
Census tract median household income, median (25^{th}-75^{th} percentile)	$77,321 ($62,003 - $94,601)	$61,228 ($42,112 - $72,268)
Insurance		
Private only	70 (40%)	19 (44%)
Any subsidized	103 (59%)	24 (56%)
Marital status		
Currently married/partnered	99 (56%)	28 (65%)
Single/Widowed/divorced/separated	77 (44%)	15 (35%)
Family support		
Yes	93 (53%)	27 (63%)
No	83 (47%)	16 (37%)
Tumor stage		
Stage I	121 (69%)	28 (65%)
Stage II	38 (22%)	12 (28%)
Stage III	15 (9%)	3 (7%)
Stage IV	2 (1%)	0 (0%)
Triple negative		
Yes	16 (9%)	8 (19%)
No	160 (91%)	35 (81%)
Hormone receptor positivity		
ER and/or PR positive	156 (89%)	33 (77%)
No	20 (11%)	10 (23%)
Multiple biopsy (Yes)		
Yes	21 (12%)	7 (16%)
No	155 (88%)	36 (84%)
Family history of breast cancer		
Yes	81 (46%)	17 (40%)
No	93 (53%)	25 (60%)
Prior history of breast cancer treatment		
Yes	17 (10%)	5 (12%)
No	158 (90%)	38 (88%)
Comorbidity		
Charlson score 0	114 (65%)	23 (53%)
Charlson score 1-8	61 (35%)	20 (47%)

Data shown as mean ± SD or median (25^{th}-75^{th} percentiles) or n (%).

Table 3.6 Factors associated with meeting the 45-day time-to-surgery benchmark

Patient characteristic	Univariable analysis OR (95%CI)	Adjusted OR (95%CI)
Age (5-year older)	**1.20 (1.06 - 1.37)**	**1.30 (1.12 - 1.53)**
Race		
White	1	
Black/African-American	0.86 (0.33 - 2.49)	
All others	0.69 (0.31 - 1.63)	
Language		
English	1	
Non-English	0.97 (0.41 - 2.57)	
Median household income by census tract ($5000 increment)	**1.11 (1.04 - 1.19)**	**1.11 (1.03 - 1.19)**
Insurance		
Private only	1	1
Any subsidized	1.16 (0.58 - 2.28)	0.95 (0.41 - 2.18)
Marital status		
Currently married/partnered	1	
Single/widowed/divorced/separated	1.41 (0.84 - 2.40)	
Family support		
No support	1	
Has support	0.66 (0.33 - 1.30)	
Tumor stage		
Stage I	1	
Stage II	0.73 (0.35 - 1.62)	
Stage III	1.15 (0.35 - 5.23)	
Stage IV	-------	
Triple negative		
Not triple negative	1	
Triple negative	0.44 (0.17 - 1.15)	
Hormone receptor positivity		
ER and/or PR positive	1	
Negative	2.36 (0.98 - 5.42)	
Multiple biopsy		
No	1	
Yes	0.70 (0.29 - 1.88)	
Family history of breast cancer		
No	1	1
Yes	1.28 (0.65 - 2.57)	1.44 (0.67 - 3.18)
Prior history of breast cancer treatment		
No	1	1
Yes	0.82 (0.30 - 2.61)	0.41 (0.11 - 1.71)
Comorbidity Score		
Charlson score 0	1	1
Charlson score 1-8	0.62 (0.31 - 1.21)	0.56 (0.25 - 1.25)

Associations with p<0.05 are in bold. 174 cases were included in the multivariable regression model and 45 cases were excluded due to missingness.

3.3 Metrics for patients' acceptance of recommended breast cancer treatment

Acceptance by a single modality is summarized in **Table 3.7**. Surgery had the highest acceptance rate of 97%. Neoadjuvant therapy, radiation, and hormone therapy had similar acceptance rates of 74%, 83%, and 85%, respectively. Chemotherapy had the lowest acceptance rate 71%. Overall, 61% of patients accepted all recommended treatment plan (**Table 3.8)**. No factors were found to be significantly associated with "All-acceptance" **(Table 3.9 and appendix Table 5.7**).

Table 3.7 Summary of acceptance by a single modality

Acceptance outcome	NeoAdjuvant therapy (n=23)		Surgery (n=240)		Radiation (n=157)		Chemotherapy (n=119)		Hormone Therapy (n=183)	
Accepted	17	74%	232	97%	130	83%	85	71%	155	85%
Not accepted	2	9%	2	0.5%	13	8%	25	21%	11	6%
Incomplete case	4	17%	6	2.5%	14	9%	9	8%	17	9%

Table 3.8 Summary of overall acceptance

Overall acceptance	N=238*	
All accepted (all recommended treatment accepted)	146	61%
Not all accepted (not all recommended treatment accepted)	49	21%
Incomplete cases (has some incomplete information of treatment)	43	18%

*9 cases who did not initiate treatment and 1 case whose treatment status could not be determined are not included for overall outcome analysis.

Table 3.9 Comparison between the all-accepted and not-all-accepted groups.

Patient characteristic	All accepted (n=146)	Not All accepted (n=49)
Age(years), mean (sd)	59 (13)	63 (13)
Race		
White	95 (65%)	34 (69%)
Black/African-American	22 (15%)	6 (12%)
All others	28 (19%)	9 (18%)
Language		
English	125 (86%)	41 (84%)
Non-English	21 (14%)	8 (16%)
Median household income by census tract, median(25^{th} -75^{th} percentile)	76,370 (59,014-90,960)	70,547 (53,705-95,480)
Insurance		
Private Only	62 (42%)	15 (31%)
Any subsidized	82 (56%)	33 (68%)
Marital status (Currently married/partnered)	62 (42.2%)	22 (44.9%)
Family support (Yes)	86 (59%)	25 (51%)
Tumor stage		
Stage I	88 (60%)	37 (76%)
Stage II	38 (27%)	5 (10%)
Stage III	15 (10%)	5 (10%)
Stage IV	5 (3%)	2 (3%)
Triple negative (Yes)	20 (14%)	5 (10%)
Hormone receptor positivity (ER and/or PR +)	124 (84%)	44 (90%)
Multiple biopsy (Yes)	20 (14%)	5 (10%)
Family history of breast cancer (Yes)	67 (46%)	25 (51%)
Prior history of breast cancer treatment (Yes)	11 (8%)	6 (12%)
Comorbidity		
Charlson score 0	88 (60%)	34 (69%)
Charlson score 1-8	58 (40%)	15 (31%)

Data shown as mean ± SD or median (25th, 75th percentiles) or n (%). Univariable and multivariable analyses were conducted to assess factors associated with non-acceptance (Appendix Table5.7). No significant factor was found to be associated with all-acceptance.

4. Discussion

4.1 Summary

Patients' acceptance of recommended treatment is a dynamic and multifactorial process that involves participation of patients, patients' social support, and health professionals. It may be influenced by multiple non-disease-related factors, such as socioeconomic status, race/ethnicity factors, language, culture, and education. This study evaluated both timeliness of breast cancer care and patients' acceptance of recommended treatment by a single modality and for all modalities in incident breast cancer. In the study population, 89% (219/247) of patients had surgery recommended as the first modality and 80% of them met the 45-day time-to-surgery benchmark. We identified that older age and higher household income by census tract were associated with timely initiation of surgery. Similarly, among 150 Stage I-III hormone receptor-positive breast cancer patients, 92% met the 365-day time-to-initiation of hormone therapy benchmark. Case review of individual patients with delays in treatments found that clinical complexity, insurance issues, and personal/family issues were some of the reasons for treatment delay.

In addition to the 45-day time-to-surgery and the 365-day time-to-initiation of hormone therapy benchmarks, we also evaluated three other established timeliness benchmarks, which revealed similar patterns (**Appendix Table 5.4**). Specifically, because surgery was the predominant first recommended treatment in our study population (89%), the 60-day benchmark showed similar results as the 45-day benchmark.

Most previous studies have been limited by evaluating acceptance of a single modality due to complexity of breast cancer treatment regimens. In this study, we assessed acceptance of care at individual modality, as reported by others, as well as overall acceptance by integrating the acceptance outcome from a single modality. In our

study, we found acceptance rates by a single modality ranged from 71% (chemotherapy) to 97% (surgery). However, when we examined acceptance across modalities, we found only 61% of patients accepted all recommended treatments. Equally striking is the number of incomplete cases (n=43, 18%); only few cases had incomplete information in more than one modality. The study findings may help us identify the high-risk patient populations of delaying and non-acceptance of recommended treatments and inform the development of interventions and policies that are aimed toward improving timely and quality of care for breast cancer patients.

4.2 Reasons of delay and potential interventions to avoid the delay

We identified several common themes across patients who experienced delays in treatment initiation by day 45 and/or day 365. After reviewing the top decile of surgery delays (n=21) and all hormone therapy delays (n=7), we categorized the reasons of delays into the followings: clinical complexity, seeking for a second opinion, insurance issues, treatment indecision, personal issues, and unclear reason. A potential intervention to address clinical complexity might include bringing the case back to the multi-disciplinary tumor board for consideration. In response to delays were caused by non-clinical issues, including insurance difficulties, treatment indecision, and personal issues, prompt and steady involvement of an interdisciplinary support team, including a patient navigator, a social worker, and/or financial coordination specialist, could be helpful to identify potential barriers to care and support patients through and/or beyond the completion of the planned treatment.

4.3 Evaluation of potential bias

When we analyzed potential factors associated with overall acceptance, 43 (18%) cases with incomplete information in their acceptance of any modalities were not

included in regression model due to incomplete data. To evaluate potential bias of excluding these cases, we compared patient characteristics of complete cases versus incomplete cases (**Appendix Table 5.8**). Two groups were similar in their demographics, disease characteristics, and comorbidity, except that the complete cases had about $11,000 more median household income by census tract compared to the incomplete cases.

4.4 Patients' preferences versus patients' acceptance of guideline-based recommendations

Patients with a lower stage disease may have options in treatment regimens. For example, according to the NCCN guidelines, patients with stage I-IIIA can choose lumpectomy with surgical axillary node staging or total mastectomy with surgical axillary staging and with/without reconstruction. Depending on the number of the positive axillary nodes, patients are typically recommended to receive radiation therapy to the whole breast after lumpectomy and may consider radiation to infraclavicular and supraclavicular regions and internal mammary nodes. During the data abstraction, we frequently encountered a scenario in which a patient was provided treatment options between lumpectomy with radiation versus mastectomy, and oncologists explained to patients in details the benefits and risks of each modality. Because the aim of this study focused on those non-acceptance cases, if a patient chose either alternative treatment regimen, it was considered acceptance of recommended treatment.

4.5 Limitations and strengths

This retrospective cohort study reviewed 247 stage I-IV patients presenting to Tufts MC between 2009 and 2013. Our results on timeliness and acceptance do not pertain to patients with stage 0 or unknown stage. Future studies are needed to evaluate quality

care in these subgroups. The study population was drawn from a single academic medical center that is located in a community with sizable immigrant Chinese population, which limits generalizability of study results. Data abstraction relied on perspective of the EMR on patients' acceptance of recommended treatments, which may not completely reflect the patients' point of view for recommended treatments.

Nevertheless, this study evaluated both timeliness benchmarks and acceptance of treatment by a single modality and overall treatment regimens. Previous studies have been limited by evaluating a single modality in breast cancer care possible due to the complexity of treatment regimens. The incorporation of timeliness and acceptance of each treatment modality allows us to study how patients' sequential treatment experience influences their subsequent acceptance.

5. Conclusion

This study demonstrates despite the complexity that both timeliness of care and overall acceptance of treatment recommendation are feasible to determine and informative. Future studies could use this approach to further explore how patients' sequential treatment experience informs subsequent treatment acceptance.

6. Appendix

Table 5.1 Weighted index of comorbidity

Scores	Clinical conditions
1	Myocardial infarct Congestive heart failure Peripheral vascular disease Dementia Cerebrovascular disease Chronic pulmonary disease Connective tissue disease Ulcer disease Mild liver disease Diabetes without complications
2	Hemiplegia Moderate or severe renal disease Diabetes with end organ damage Any tumor, diagnosed within prior 5 years Leukemia Lymphoma
3	Moderate or severe liver disease.
6	Metastatic solid tumor AIDS

The table was adapted from (Charlson et al., 1987; Deyo et al., 1992; Quan et al., 2005).

Figure 5.1 Distribution of Charlson Score in the study population

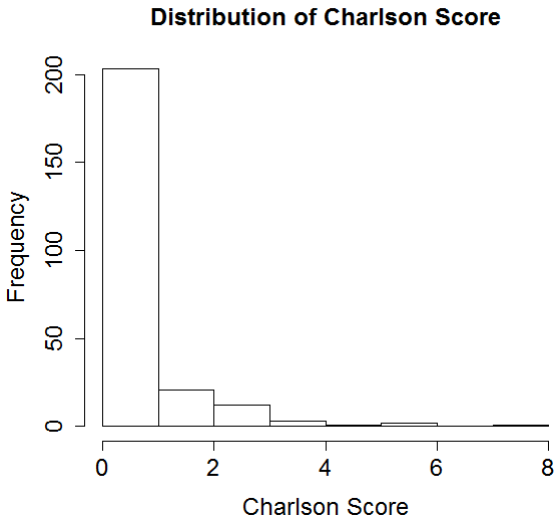


Table 5.2a Summary of missing data in patient characteristics (N=247 patients)

Patient Characteristics	Number of patients with missing information	% of patients with missing information
Age	0	----
Race	1	0.4%
Language	0	----
Census Tract to assess Median household income	11	4.5%
Insurance	7	2.8%
Marital status	0	----
Family support	0	----
Tumor stage	0	----
Triple negative	1	0.4%
Hormone receptor positivity	1	0.4%
Multiple biopsy	0	----
Family history of breast cancer	4	1.6%
Prior history of breast cancer treatment	1	0.4%
Charlson Comorbidity Score	1	0.4%

Table 5.2b Summary of missing data in outcomes

Outcomes	Benchmarks	Evaluable cases for benchmarks	Total No.	Missing No.
Timeliness benchmark	45-day time-to-surgery	Patients with surgery recommended as the first treatment	219	0
	365-day time-to-hormone therapy	Patients with Stage I-III hormone receptor-positive breast cancer and with hormone therapy recommended	150	5
	60-day benchmark of initiation	Patients who initiated treatment at TMC	238	0
	120-day time-to-chemotherapy	Stage I-III triple negative breast cancer with adjuvant chemotherapy	15	1
	365-day time-to-radiation therapy	Patients who reveived breast-conserving surgery and were recommended radiation therapy	109	0
Acceptance by a single modality	NeoAdjuvant	Patients with neoadjuvant chemotherapy recommended	23	4
	Surgery	Patients with surgery recommended	240	6
	Radiation	Patients with radiation therapy recommended	157	14
	Chemotherapy	Patients with adjuvant chemotherapy recommended	119	9
	Hormone Therapy	Patients with hormone therapy recommended	183	17
Overall acceptance	Accepted all recommended modalities	Patients who initiated treatment at TMC	238	43

Table 5.3 Evaluable cases for timeliness of inititation of hormone therapy

<table>
<tr><th>Hormone therapy recommended</th><th colspan="3">Patient accepted hormone therapy*</th></tr>
<tr><td rowspan="5">Yes (n=183)</td><td colspan="3">No (n=11)</td></tr>
<tr><td rowspan="3">Yes (n=155)</td><td>stage I (n=100)</td><td rowspan="3">n=150 evaluable cases for this benchmark</td></tr>
<tr><td>stage II (n=39)</td></tr>
<tr><td>stage III (n=11)</td></tr>
<tr><td colspan="2">Stage IV (n=5)</td></tr>
<tr><td colspan="3">Unknown (n=17)</td></tr>
</table>

*stage I-III ER+/PR+

Table 5.4 Quality benchmarks for timeliness of care for initiation of any treatment, adjuvant chemotherapy, and radiation therapy

Treatment Benchmarks	N (%)	Median days (25^{th} - 75^{th} percentiles)
60-day benchmark of initiation of treatment (N=238)		
< = 60 days	213 (89)	29 (18 - 41)
> 60 days	25 (11)	
Stage I-III triple negative breast cancer with adjuvant chemotherapy (N=15)		
< = 120 days	11 (73)	84 (75 - 103)
> 120 days	3 (20)	
Unknown	1 (7)	
Patient received breast-conserving surgery with radiation therapy (N = 109)		
< = 365 days	100 (92)	132 (70 - 201)
> 365 days	9 (8)	

Table 5.5 Patient characteristics by 60-day benchmark (N=238)

Patient characteristic	Meeting benchmark <= 60 days (N = 213)		Not meeting benchmark >60 days (N = 25)	
Mean age, y(sd)	61 (13)		58 (14)	
Race/ethnicity				
White	143	(67%)	18	(72%)
Black/African-American	30	(14%)	2	(8%)
All others	39	(18%)	5	(20%)
Language				
English	180	(85%)	22	(88%)
Non-English	33	(15%)	3	(12%)
Census tract median household income, median (25^{th} - 75^{th} percentile)	$75,930 ($60,460 - $93,023)		$60,950 ($39,913 - $65,812)	
Insurance*				
Private only	83	(39%)	11	(44%)
Any subsidized	124	(58%)	13	(52%)
Marital status				
Currently married/partnered	119	(56%)	16	(64%)
Single/Widowed/divorced/separated	94	(44%)	9	(36%)
Family support				
Yes	121	(57%)	13	(52%)
No	92	(43%)	12	(48%)
Tumor stage				
Stage I	136	(64%)	14	(56%)
Stage II	49	(23%)	6	(24%)
Stage III	20	(9%)	4	(16%)
Stage IV	8	(4%)	1	(4%)
Triple negative				
Yes	26	(12%)	4	(16%)
No	187	(88%)	21	(84%)
Hormone receptor positivity				
ER and/or PR positive	182	(85%)	20	(80%)
No	31	(15%)	5	(20%)
Multiple biopsy (Yes)				
Yes	29	(14%)	6	(24%)
No	184	(86%)	19	(76%)
Family history of breast cancer				
Yes	98	(46%)	12	(48%)
No	111	(52%)	13	(52%)
Prior breast cancer treatment				
Yes	21	(10%)	1	(4%)
No	191	(90%)	24	(96%)
Comorbidity				
Charlson score 0	132	(62%)	17	(68%)
Charlson score 1-8	80	(38%)	8	(32%)

Data shown as mean ± SD or median (25th, 75th percentiles) or n (%).

Table 5.6 Factors associated with meeting the 60-day benchmark.

Patient characteristic	Univariable Models OR (95%CI)	Multivariable Model OR (95%CI) N=207*
Age (5-year older)	1.08 (0.93 - 1.27)	1.09 (0.91 - 1.31)
Race		
White	1	
Black/African-American	1.89 (0.51 - 12.3)	
All others	0.98 (0.36 - 3.12)	
Language		
English	1	
Non-English	1.34 (0.43 - 5.90)	
Median household income ($5000 increment)	**1.10 (1.02 - 1.20)**	**1.12 (1.03 - 1.23)**
Insurance		
Private only	1	1
Any subsidized	1.26 (0.53 - 2.96)	1.36 (0.48 - 3.84)
Marital status		
Currently married/partnered	1	
Single/widowed/divorced/separated	1.05 (0.56 - 1.98)	
Has family support		
No support	1	
Has support	1.21 (0.52 - 2.80)	
Tumor stage		
Stage I	1	
Stage II	0.84 (0.32 - 2.48)	
Stage III	0.51 (0.16 - 1.95)	
Stage IV	0.82 (0.14 - 15.85)	
Triple negative		
Not triple negative	1	
Triple negative	0.73 (0.25 - 2.64)	
Hormone receptor positivity		
ER and/or PR positive	1	
Negative	1.47 (0.25 - 2.65)	
Multiple biopsy		
No multiple biopsy	1	
Has multiple biopsy	0.50 (0.19 - 1.46)	
Family history of breast cancer		
No	1	1
Yes	0.96 (0.41 - 2.22)	0.90 (0.35 - 2.32)
Prior history of breast cancer treatment		
No	1	1
Yes	2.64 (0.51 – 48.34)	1.91 (0.31 - 37.4)
Comorbidity		
Charlson score 0	1	1
Charlson score 1-8	1.29 (0.55 - 3.28)	2.00 (0.71 – 6.57)

p<0.05 is in bold. *31 observations were deleted due to missingness.

Table 5.7 Factors associated with all-acceptance of recommended treatments

Patient characteristic	Univariable analysis OR (95%CI)	Adjusted OR (95%CI) N=180*
Age (5-year)	**0.85 (0.75 - 0.97)**	0.87 (0.74 - 1.00)
Race		
White	1	
Black/African-American	1.31 (0.52 - 3.80)	
All others	1.11 (0.49 - 2.71)	
Language		
English	1	
Non-English	0.86 (0.37 - 2.20)	
Median household income ($5000 increment)	0.99 (0.94 - 1.04)	0.98 (0.93 - 1.04)
Insurance		
Private only	1	1
Any subsidized	0.61 (0.30 - 1.20)	0.72 (0.31 - 1.64)
Marital status		
Currently married/partnered	1	
Single/widowed/divorced/separated	0.90 (0.47 - 1.74)	
Has family support		
No support	1	
Has support	1.38 (0.72 - 2.64)	
Tumor stage		
Stage I	1	
Stage II	3.20 (1.26 - 9.80)	
Stage III	1.25 (0.45 - 4.10)	
Stage IV	1.05 (0.22 - 7.56)	
Triple negative		
Not triple negative	1	
Triple negative	1.40 (0.53 - 4.40)	
Hormone receptor positivity		
Negative	1	
ER and/or PR positive	0.61 (0.19 - 1.58)	
Has Multiple biopsy		
No multiple biopsy	1	
Has multiple biopsy	1.40 (0.53 - 4.40)	
Has family history of breast cancer		
No	1	1
Yes	0.84 (0.44 - 1.60)	0.91 (0.45 - 1.82)
Has prior history of breast cancer treatment		
No	1	1
Yes	0.58 (0.21 - 1.78)	0.72 (0.23 - 2.39)
Has comorbidity		
No	1	1
Yes	1.51 (0.77 - 3.09)	1.59 (0.76 - 3.44)

p<0.05 is in bold.* 15 observations deleted due to missingness

Table 5.8 Comparison of complete cases and incomplete cases.

Patient characteristic	Complete (n=195)	Incomplete (n=43)	P value
Age, y (sd)	61 (13)	60 (15)	0.6667
Race			0.7270†
White	130 (67%)	29 (67%)	
Black/African-American	28 (14%)	4 (10%)	
All others	37 (19%)	9 (23%)	
Language			0.5327
English	167 (85%)	35 (80%)	
Non-English	28 (15%)	8 (20%)	
Census tract median household income, median (25^{th}-75^{th} percentile)	$76,090 ($57,024 - $92,644)	$65,905 ($51,127 - $76,804)	**0.0490‡**
Insurance			0.4132
Any private	77 (39%)	19 (45%)	
Subsidized	115 (59%)	21 (49%)	
Marital status			0.9543
Currently married/partnered	112 (57%)	26 (59%)	
Single/widowed/divorced/separated	84 (43%)	17 (41%)	
Family support			0.9494
Yes	111 (57%)	23 (55%)	
Tumor stage			0.2535†
Stage I	125 (64%)	22 (51%)	
Stage II	44 (22%)	12 (31%)	
Stage III	20 (10%)	4 (10%)	
Stage IV	6 (4%)	3 (8%)	
Triple negative (Yes)			0.8438†
Not triple negative	171 (87%)	36 (84%)	
Triple negative	24 (13%)	5 (14%)	
Hormone receptor positivity			0.4361
Negative	27 (14%)	8 (20%)	
ER and/or PR positive	168 (86%)	34 (79%)	
Multiple biopsy (Yes)			0.1719
Yes	25 (13%)	9 (22%)	
Family history of breast cancer			0.5372
Yes	92 (47%)	16 (40%)	
Prior history of breast cancer treatment			0.7825†
Yes	17 (9%)	4 (10%)	
Comorbidity			0.7179
No (Charlson score 0)	122 (62%)	29 (67%)	
Yes (Charlson score 1-8)	73 (38%)	14 (33%)	

Student t-test was used to compare the means of age. ‡ Wilcoxon rank sum test was used to compare median household income by census tract. Chi-squared test was used to compare the categorical variables. † Fisher's exact test was used for categorical variables with any category had a count less than or equal to 5. $p<0.05$ is in bold.

Table 5.9 Comparison between stage-known and stage-unknown cases

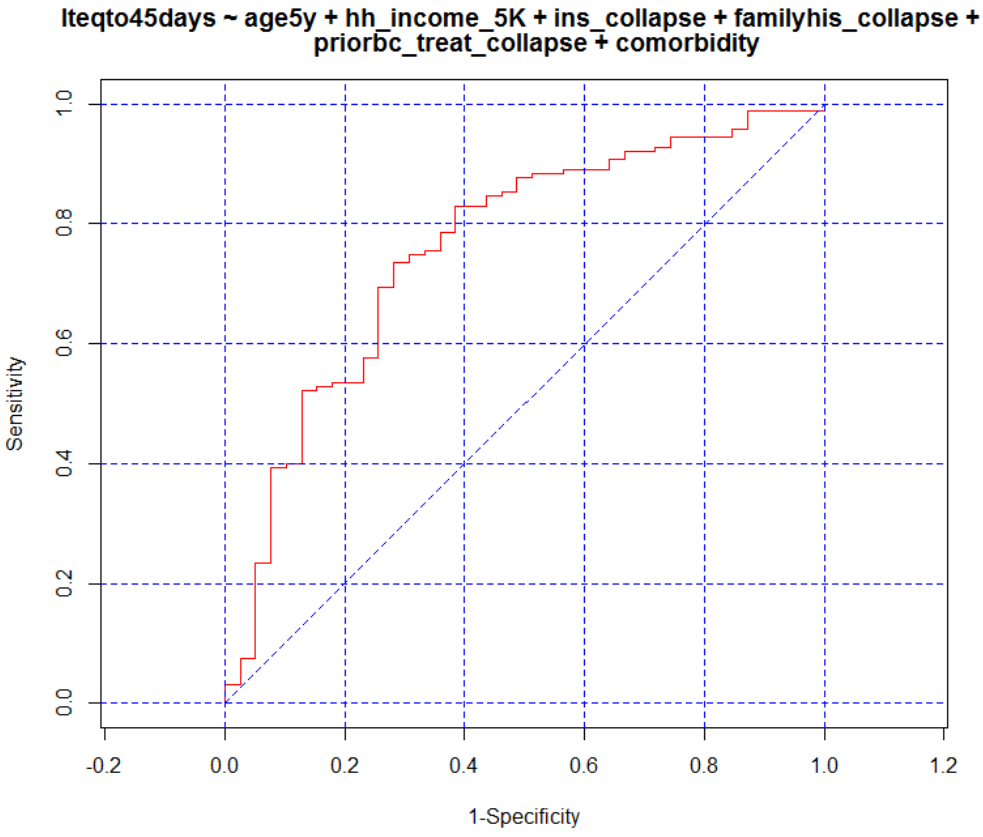
Patient characteristic	Stage known (N = 247)	Stage unknown (N = 16)	P value
Mean age, y(sd)	60 (14)	57 (11)	0.5197
Race/ethnicity			0.2000†
White	164 (66%)	11 (69%)	
Black/African-American	33 (13%)	0 (0%)	
All others	49 (20%)	5 (31%)	
Language			0.7265†
English	208 (84%)	13 (81%)	
Non-English	39 (16%)	3 (19%)	
Census tract median household income, median (25^{th}, 75^{th} percentile)	$71,452 ($56,122, $90,406)	$71,387 ($61151, $85539)	0.8192‡
Insurance			0.0654†
Private only	100 (43%)	10 (63%)	
Any subsidized	140 (56%)	5 (31%)	
Marital status			0.1988†
Currently married/partnered	142 (57%)	12 (75%)	
Single/Widowed/divorced/separated	105 (43%)	4 (25%)	
Has family support			0.4372†
Yes	139 (56%)	11 (69%)	
No	108 (44%)	5 (31%)	
Triple negative			**<0.01**†
Yes	32 (13%)	1 (6%)	
No	214 (86.6%)	10 (63%)	
Unknown	1 (0.4%)	5 (31%)	
Hormone receptor positivity			**<0.01**†
ER and/or PR positive	208 (84.2%)	9 (56%)	
No	38 (15.4%)	2 (13%)	
Unknown	1 (0.4%)	5 (31%)	
Multiple biopsy (Yes)			1†
Yes	36 (15%)	2 (13%)	
No	211 (85%)	14 (88%)	
Has family history of breast cancer			0.0324†
Yes	112 (45%)	4 (25%)	
No	131 (53%)	9 (56%)	
Has prior history of breast cancer treatment			0.6106†
Yes	22 (9%)	0 (0%)	
No	224 (91%)	13 (100%)	
Comorbidity			0.8714†
Charlson score 0	156 (63%)	11 (69%)	
Charlson score 1-8	90 (37%)	5 (31%)	

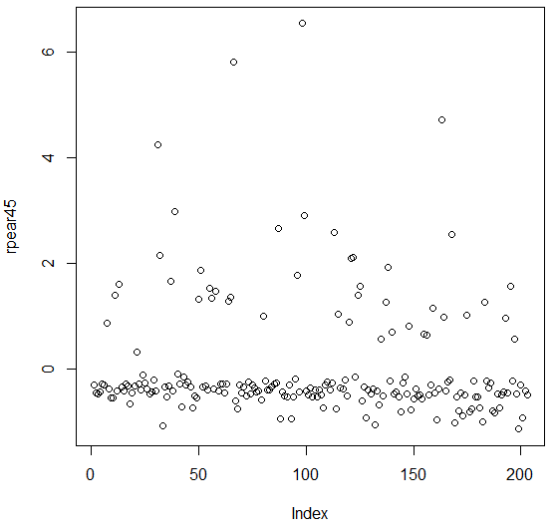
Student t-test was used to compare the means of age. ‡ Wilcoxon rank sum test was used to compare medians of census tract median household income. † Fisher's exact test was used for categorical variables with any category had a count less than or equal to 5. p<0.05 is in bold.

Model diagnosis for 45 days benchmark:

```
Frequencies of Missing Values Due to Each Variable
          lteqto45days                   age5y           hh_income_5K
         ins_collapse     familyhis_collapse
                   28                      0                     11
                    7                      4
priorbc_treat_collapse            comorbidity
                    1                      1
Logistic Regression Model
  lrm(formula = lteqto45days ~ age5y + hh_income_5K + ins_collapse +
     +familyhis_collapse + priorbc_treat_collapse + comorbidity,
     data = predata)
                      Model Likelihood     Discrimination    Rank Discrim.
                           Ratio Test           Indexes           Indexes
 Obs         202    LR chi2     23.83    R2        0.178    C         0.758
  0           39    d.f.            6    g         1.084    Dxy       0.515
  1          163    Pr(> chi2) 0.0006    gr        2.957    gamma     0.517
 max |deriv| 3e-05                       gp        0.149    tau-a     0.161
                                         Brier     0.136

                          Coef    S.E.   Wald Z Pr(>|Z|)
 Intercept               -2.8430 1.0146 -2.80  0.0051
 age5y                    0.2635 0.0804  3.28  0.0011
 hh_income_5K             0.1011 0.0355  2.85  0.0044
 ins_collapse            -0.0564 0.4268 -0.13  0.8949
 familyhis_collapse       0.3635 0.3958  0.92  0.3583
 priorbc_treat_collapse  -0.8962 0.6810 -1.32  0.1882
 comorbidity             -0.5763 0.4042 -1.43  0.1540
```

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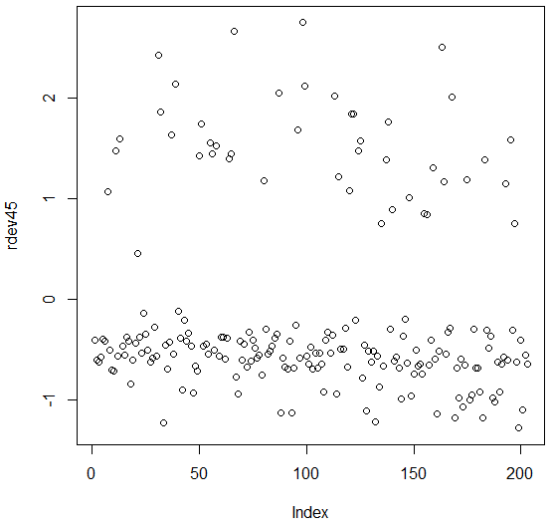
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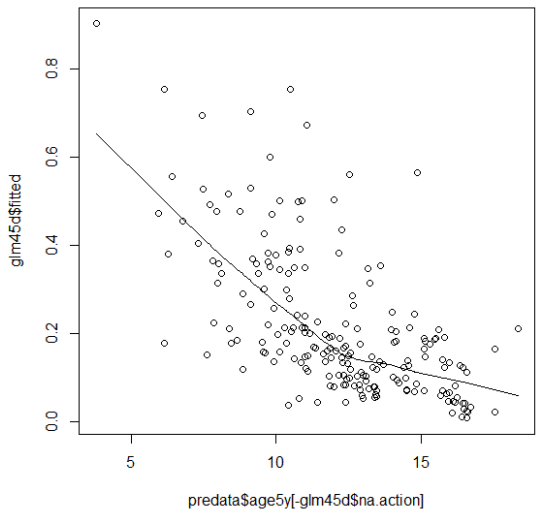
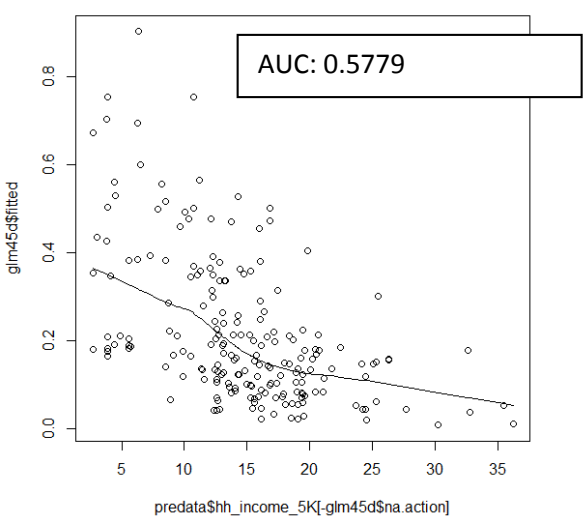
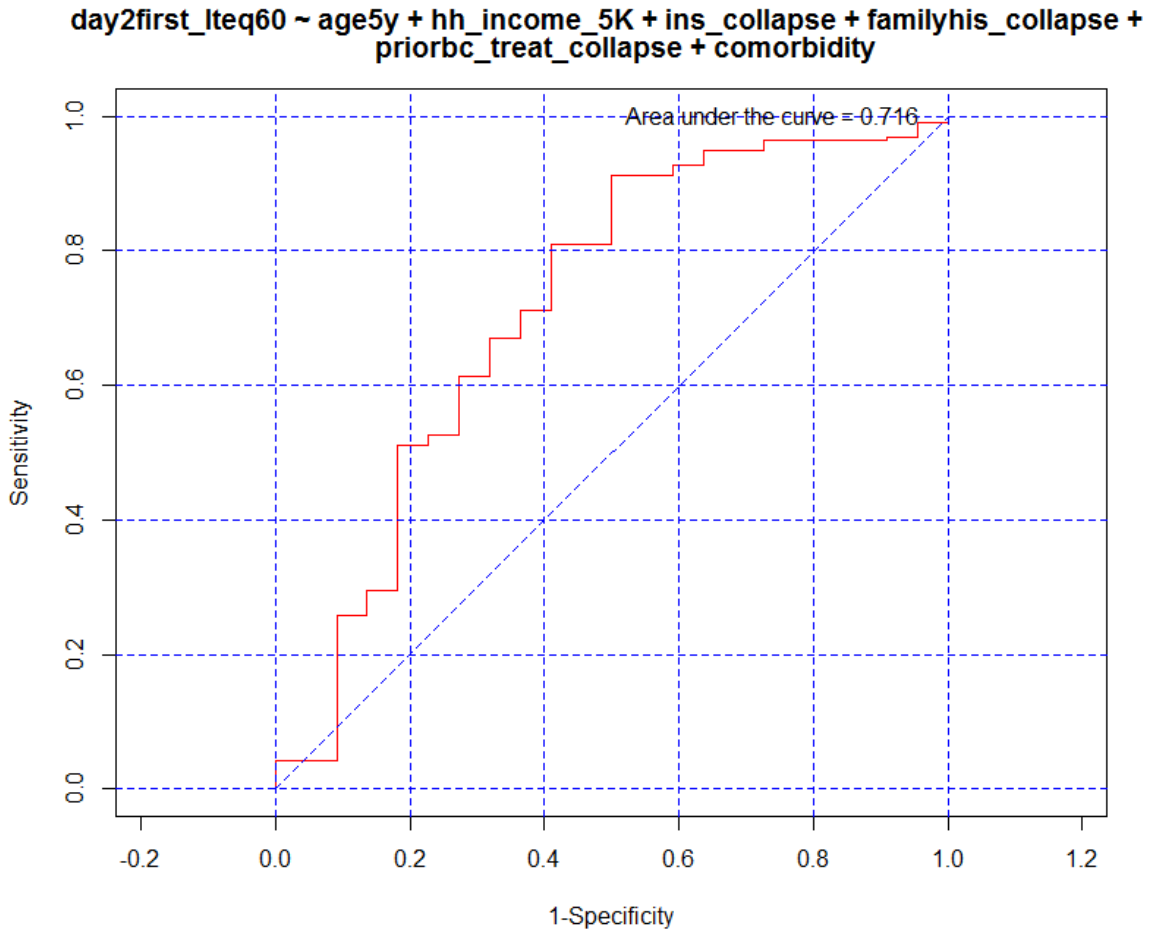
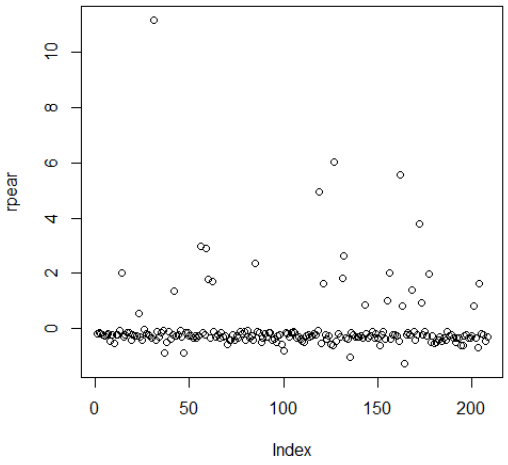

glm45d$fitted
predata$age5y[-glm45d$na.action]

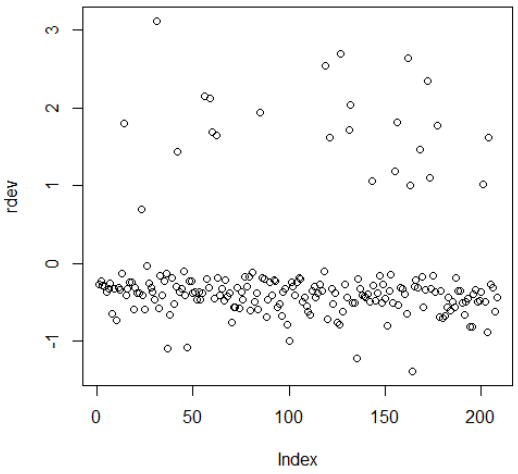

AUC: 0.5779
glm45d$fitted
predata$hh_income_5K[-glm45d$na.action]

Model diagnosis for 60-day bench mark

```
Logistic Regression Model

 lrm(formula = day2first_lteq60 ~ age5y + hh_income_5K + ins_collapse +
     familyhis_collapse + priorbc_treat_collapse + comorbidity,
     data = predata)

                       Model Likelihood     Discrimination    Rank Discrim.
                             Ratio Test           Indexes          Indexes
Obs         216    LR chi2     10.70    R2       0.100    C       0.714
 0           22    d.f.            6    g        0.918    Dxy     0.429
 1          194    Pr(> chi2) 0.0980    gr       2.503    gamma   0.432
max |deriv| 6e-05                       gp       0.074    tau-a   0.079
                                        Brier    0.085

                      Coef    S.E.   Wald Z Pr(>|Z|)
Intercept             -0.7146 1.1597 -0.62  0.5378
age5y                  0.0869 0.0928  0.94  0.3491
hh_income_5K           0.1132 0.0451  2.51  0.0121
ins_collapse           0.3014 0.5283  0.57  0.5684
familyhis_collapse    -0.1014 0.4739 -0.21  0.8305
priorbc_treat_collapse 0.6516 1.1065  0.59  0.5560
comorbidity            0.6936 0.5554  1.25  0.2117
```







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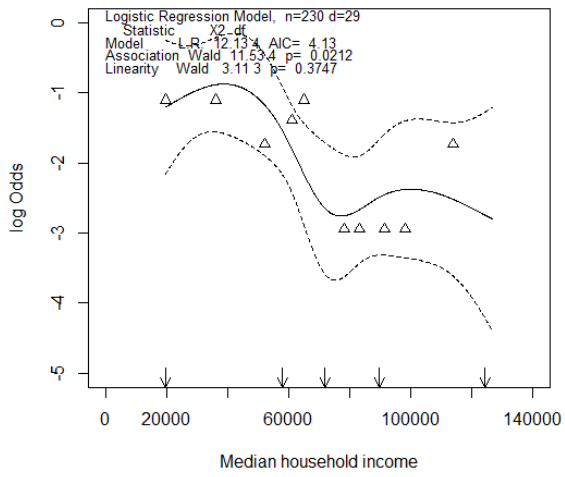
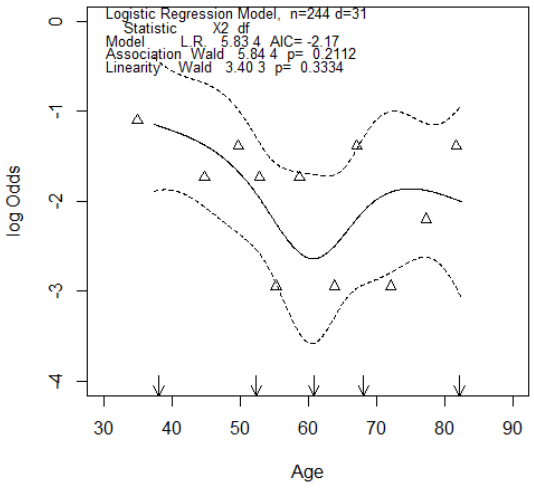
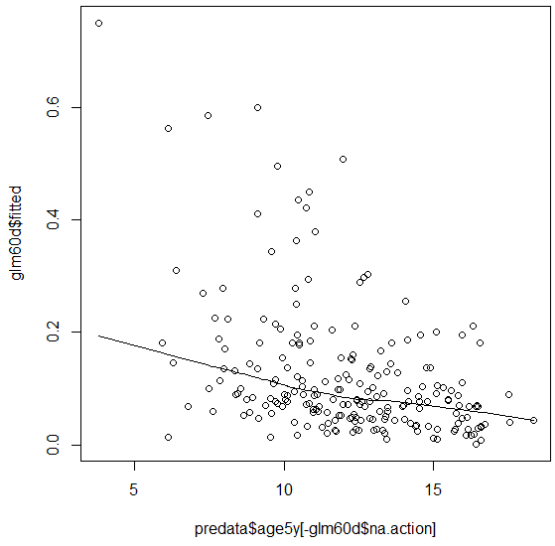


Estimated Spline Transformation





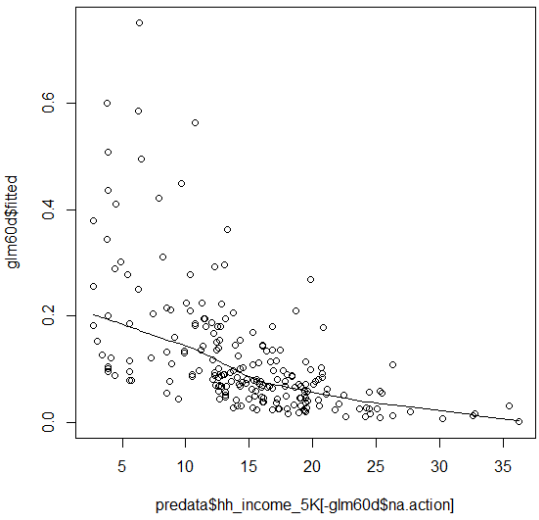


Table 1 Patient characteristics

Demographic			**Notes**
Sex	1) Male 2) Female		
Age	DOB (MM/DD/YYYY)		
Race/Ethnicity	1) White 2) Black/African American 3) Hispanic/Latino 4) Chinese origin 5) Other Asian 6) Other 7) Unknown		
Language	Native Language: 1) English 2) Mandarin 3) Cantonese 4) Other Chinese 5) All others (except Chinese and English) 6) Unknown	For a non-native English speaker (option 2-6), whether the Interpreter Service was used? ☐Yes ☐No	
Socioeconomic and household			
Health Insurance Coverage	1) Medicare 2) Medicaid / MassHealth (Medicaid in MA) 3) Dual Medicaid / Medicare 4) Private health insurance 5) Uninsured 6) Other (Please specify)		
Address	Street City: State: Zipcode:		
Family Support	Does medical record document any family members participate in visit or health care delivery? ☐Yes ☐No		
Marital Status	1) Single 2) Currently married / partnered 3) Widowed / divorced / separated 4) Unknown		
Disease Information at initial diagnosis (Dx)			
The most recent screening MAM before Dx ☐Yes ☐No If Yes (mm/dd/yyyy):		Date of prior screening MAM ☐Yes ☐No If Yes (mm/dd/yyyy):	
Diagnostic Biopsy Date: (mm/dd/yyyy)		Multiple biopsies required: ☐Yes ☐No	
Breast Cancer Staging	Anatomic Stage ☐ 0 ☐ IA ☐ IB ☐IIA ☐IIB ☐IIIA ☐IIIB ☐ IIIC ☐IV	TNM stage system T N M	
Tumor Biology	1) ER ☐ Positive ☐ Negative 2) PR ☐ Positive ☐ Negative 3) HER2 ☐ Positive ☐ Negative ☐Equivocal 4) Triple negative ☐ Yes ☐ No	If ER+ and/or PR+, and HER2- ☐Yes (Oncotype score=) ☐No ☐Not stated	
Treatment Regimens	Recommended by Physician / Received by Patient		
	1) Surgery ☐Yes ☐No ☐Not stated / ☐Yes ☐ No ☐ Unknown 2) Radiation ☐Yes ☐No ☐Not stated / ☐Yes ☐ No ☐ Unknown 3) Neoadj Chemo ☐Yes ☐No ☐Not stated / ☐Yes ☐ No ☐ Unknown 4) Chemotherapy ☐Yes ☐No ☐Not stated / ☐Yes ☐ No ☐ Unknown 5) Hormone Rx ☐Yes ☐No ☐Not stated / ☐Yes ☐ No ☐ Unknown 6) Exercise Rx ☐Yes ☐No ☐Not stated / ☐Yes ☐ No ☐ Unknown		
	For patients with stage 0 cancer, whether an active surveillance or screening was recommended? ☐Yes ☐ No If yes, when was the first surveillance? (mm/dd/yyyy)		
Comorbidities and Family History	Please check the list of comorbidities attached: ☐ I have Checked the list	Family history of breast cancer or ovarian cancer: ☐Yes ☐No ☐Not stated ☐ Unknown	
	Prior history of breast cancer treatment ☐Yes ☐No ☐ Unknown If yes, please record the year (yyyy)		
Enrollment in Clinical Trial	Was a clinical trial recommended? ☐Yes ☐ No ☐ Unknown Was patient enrolled? ☐Yes ☐ No ☐ Unknown		

Table 2 Recommended Treatments

Surgery							**Summary**	
Recommended Surgery ☐ Tufts Medical Center ☐ Outside facility				**Surgery Received** ☐ Tufts Medical Center ☐ Outside facility		**Actually occurred date (mm/dd/yyyy)**	**Any documented delay**	**Any changes in surgery**
☐ Lumpectomy ☐ Mastectomy			☐Left ☐Right ☐Bilateral	☐ Lumpectomy ☐ Mastectomy	☐Left ☐Right ☐Bilateral		☐ Yes ☐ No	☐ Yes ☐ No
Re-excision	1	☐ Yes ☐ No	Reason:	☐ Yes ☐ No			☐ Yes ☐ No	☐ Yes ☐ No
	2	☐ Yes ☐ No	Reason:	☐ Yes ☐ No			☐ Yes ☐ No	☐ Yes ☐ No
	3	☐ Yes ☐ No	Reason:	☐ Yes ☐ No			☐ Yes ☐ No	☐ Yes ☐ No
Notes:								

Radiation Therapy			
Actual delivery ☐ Tufts Medical Center ☐ Outside facility		**Any documented interruption during the therapy**	**Reasons for interruption**
Actual starting date		☐ Yes ☐ No	
Actual cumulative dose			
Actual completion date			
Notes:			

Hormonal therapy					
Actual delivery ☐ Tufts Medical Center ☐ Outside facility		**Any delay in start**	**Reasons for delay**	**Any Interruption after start**	**Reasons for interruption**
Actual medication	**Actual starting date**				
		☐ Yes ☐ No		☐ Yes ☐ No	
		☐ Yes ☐ No		☐ Yes ☐ No	
		☐ Yes ☐ No		☐ Yes ☐ No	
Notes:					

Chemotherapy

Neoadj Chemotherapy

Regimen	**Actual delivery**		**Any interruptions during the treatment** ☐ Yes ☐ No		
Recommended regimen: ☐ Tufts Medical Center ☐ Outside facility	☐ Tufts Medical Center ☐ Outside facility		**No.**	**Date of the interruption (mm/dd/yyyy – mm/dd/yyyy)**	**Reasons for the interruption**
	Start date (mm/dd/yyyy)	**End date (mm/dd/yyyy)**	**1**		
			2		
	Any delay at the start ☐ Yes ☐ No		**3**		
	Reason(s) for the delay:		**4**		
			5		
			6		

Chemotherapy

Regimen 1	**Actual delivery**		**Any interruptions during the treatment** ☐ Yes ☐ No		
Recommended regimen: ☐ Tufts Medical Center ☐ Outside facility	☐ Tufts Medical Center ☐ Outside facility		**No.**	**Date of the interruption (mm/dd/yyyy – mm/dd/yyyy)**	**Reasons for the interruption**
	Start date (mm/dd/yyyy)	**End date (mm/dd/yyyy)**	**1**		
			2		
	Any delay at the start ☐ Yes ☐ No		**3**		
	Reason(s) for the delay:		**4**		
			5		
			6		

Regimen 2	**Actual delivery**		**Any interruptions during the treatment** ☐ Yes ☐ No		
Recommended regimen: ☐ Tufts Medical Center ☐ Outside facility	☐ Tufts Medical Center ☐ Outside facility		**No.**	**Date of the interruption (mm/dd/yyyy – mm/dd/yyyy)**	**Reasons for the interruption**
	Start date (mm/dd/yyyy)	**End date (mm/dd/yyyy)**	**1**		
			2		
	Any delay at the start ☐ Yes ☐ No		**3**		
	Reason(s) for the delay:		**4**		
			5		
			6		

Regimen 3	**Actual delivery**		**Any interruptions during the treatment** ☐ Yes ☐ No		
Recommended regimen: ☐ Tufts Medical Center ☐ Outside facility	☐ Tufts Medical Center ☐ Outside facility		**No.**	**Date of the interruption (mm/dd/yyyy – mm/dd/yyyy)**	**Reasons for the interruption**
	Start date (mm/dd/yyyy)	**End date (mm/dd/yyyy)**	**1**		
			2		
	Any delay at the start ☐ Yes ☐ No		**3**		
	Reason(s) for the delay:		**4**		
			5		
			6		

Notes:

If the last visit of the patient occurred within 1 year since diagnosis, please record the date of the last visit note (mm/dd/yyyy):

Notes:

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