The Economic Consequences of Breast Cancer Adjuvant Hormonal Treatments

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RATIONALE: Adjuvant hormone therapy (HT) based on tamoxifen (TX) or aromatase inhibitors (AIs) has become the standard of care for treating hormone receptor -positive (HR+) breast cancer (BC) over the past 20 years. Based on clinical trial results, AI use is recommended by the American Society of Clinical Oncology for treatment of postmenopausal women with HR+ breast cancer. AIs, however, are significantly more expensive than TX, raising concerns about access and use of effective treatment among women of lower socio-economic status.

OBJECTIVES: To examine the relationship between adjuvant HT modality and experience of financial hardship among a cohort of older BC survivors. Also, to examine the extent to which financial concerns affect the probability of switching between adjuvant HT modalities.

DESIGN: Population-based, prospective survey study.

PARTICIPANTS: Elderly (65+) women who had an incident BC surgery in 2003 and who reported receiving adjuvant HT during the first 12 months post-surgery.

METHODS: Multivariate regression models.

RESULTS: Use of AIs was associated with a significantly higher probability of financial hardship. Women who had taken only an AI were more likely to experience financial difficulty than women who took only TX (OR=1.4; 95% CI: 1.1–1.7), but women who switched between TX and AI were not more likely to experience financial difficulty. Breast cancer survivors with no drug coverage (OR=4.5; 95% CI: 3.3–5.9) or partial drug coverage (OR=3.6; 95% CI: 2.8–4.5) were more likely to experience financial difficulty compared to those with full coverage. Lack of drug coverage was also the main factor associated with the likelihood that BC survivors did not switch adjuvant HT modalities.

CONCLUSIONS: Adjuvant HTs have important economic consequences for BC survivors. These consequences are ameliorated by full, but not partial, drug coverage.

KEY WORDS: homonal therapy; tamoxifen; aromatase inhibitors; breast cancer; treatment.
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INTRODUCTION

Hormonal therapy with tamoxifen (TX) and, more recently, aromatase inhibitors (AIs) has become an integral part of breast cancer treatment among women with hormone receptor- positive (HR+) breast cancer over the past 20 years. Until recently, TX had been the hormonal therapy of choice for the adjuvant therapy of early stage breast cancer. However, the greater effectiveness of AIs compared to TX in reducing disease recurrence has been demonstrated in several recent clinical trials including trials comparing 5-year monotherapy with an AI to TX[1]as well as switching from TX to an AI after 2–3 years [2–4]. Evidence suggests that AIs improve disease-free survival by reducing distant metastases by 61% and contralateral breast cancers by 80% compared to TX [1–3]. An additional benefit of the AIs is the reduction in several commonly recognized adverse-effects of TX, including thromboembolism and endometrial carcinoma [3]. The main negative side effect of AIs is an increased risk of osteoporosis, a treatable condition. Given these results, the American Society of Clinical Oncology (ASCO) has since 2004 recommended that adjuvant treatment for postmenopausal women with HR+ breast cancer should include an AI.[5] Although recognizing that, because of the lack of a demonstrated survival advantage to AIs, "TX remains a reasonable alternative," the National Cancer Institute (NCI) states in its Health Professional guidelines that AIs have become the first-line adjuvant therapy for postmenopausal women [6]. Consistent with these statements, the National Comprehensive Cancer Network (NCCN) recommends use of TX alone only in instances where women have a contra-indication to, are intolerant of, or decline AIs [7]. Because a large majority of breast cancer patients have postmenopausal disease, and about 75% of these have HR+ tumors, [8–11] these recommendations are applicable to a majority of the women developing breast cancer annually.

AIs, however, are not available in generic formulations, and are 8–10 times more expensive than TX. The annual cost of an AI is around $2700 to $3500 compared to $240 to $360 for TX.[12] Although evidence suggests that the financial burden of disease for women with BC can be considerable, even among

those with traditional health insurance policies,[13] little is known about the economic consequences of adjuvant hormonal BC treatment or the extent to which financial factors are associated with persistence of adjuvant treatment regimes during the course of the disease. Taking advantage of a large, representative survey of women aged 65 or older with incident breast cancer in 2003, we examine the relationship between adjuvant HT modality and experience of financial hardship among a cohort of older BC survivors and the extent to which financial factors affect BC survivors' likelihood of switching between adjuvant HT modalities. We hypothesize that women using AIs will be more likely to experience financial hardship than BC survivors treated with TX, even after controlling for a wide array of socio-demographic and economic characteristics. We also anticipate that women with more robust drug insurance coverage will be less likely to experience such hardships and be more likely to switch treatment regimes than those with only limited or no prescription drug coverage.

METHODS

Data Sources

Data source for the study was the "Improving the Care and Outcomes of Women Undergoing Breast Surgery," a population-based, longitudinal survey of community-dwelling elderly women with incident breast cancer in 2003. The survey was targeted to obtain information on socio-demographic and treatment factors, and the economic and health outcomes of breast cancer care and was conducted in four states—California, Florida, Illinois and New York—that were selected based on geographic and racial-ethnic diversity. Details about the survey are provided in Nattinger et al. [14]. Briefly, women were initially identified from Medicare claims as having incident breast cancer in 2003. Potentially eligible participants were then contacted by mail in 2005 and four subsequent annual structured telephone interviews conducted by trained interviewers were fielded using procedures approved by the Centers for Medicare and Medicaid Services (CMS) and by the appropriate Institutional Review Boards.

For the purpose of this analysis, the sample consists of the subset of adjuvant HT users who participated in the initial survey (2005), roughly 30 months post-incident breast surgery. The overall participation rate for the initial wave of the survey was 70% [14].

Variable Definitions

The dependent variables examined in this study were (i) the experience of health-related financial problems and (ii) the probability of switching HT modalities during the study period. Experience of health-related financial difficulties was based on self-reported information about the degree of difficulty paying for medical bills, including breast cancer prescribed medications, during the past 12 months obtained using a Likert scale approach [15]. Women who indicated that it was "somewhat difficult" or "very difficult" to pay medical bills were classified as experiencing health-related financial difficulties.

Adjuvant hormonal therapy modality was based on self-reported use of tamoxifen or an AI (specifically, anastrozole, letrozole, or exemestane) that began within the first 12 months from the incident breast cancer surgery. Our rationale for the one-year threshold is based on recommendations by the National Comprehensive Cancer Network (NCCN) on breast cancer quality which recommends that patients with hormone receptor-positive cancers over one cm in size and/or have lymph node involvement be considered or receive hormonal therapy within 12 months of diagnosis.[6] Women were categorized in three mutually exclusive groups as (i) using adjuvant HT with tamoxifen only, (ii) using adjuvant HT with AIs only, or (iii) using both tamoxifen and AIs (i.e., women who switched regimen) during the study period (about 30 months post-incident breast cancer surgery).

Information on age and state of residence was derived from Medicare enrollment files. The presence and number of comorbid conditions was characterized by examining individual's inpatient, outpatient and Carrier claims for the period between incident breast surgery and survey interview using the methodology described in Klabunde.[16] Most other information came from the patient interviews. Women were classified according to their reported race/ethnicity as White non-Hispanic, Black/African American non-Hispanic, Hispanic, or other race/ethnicity. Marital status categories were married/living with a partner, widowed, separated/divorced, and never married. Educational level was captured by years of formal education and categorized as less than high school, high school graduate, and some college. Respondents were also asked to estimate their annual household income in the year preceding the survey. Income was then classified in categories as $15,000 or less, $15,001–$30,000, $30,001–$45,000, and greater than $45,000. Finally, prescription drug coverage was based on how much of the cost of prescription medications was covered by health insurance plans and was defined as: none; partial, if the plan paid for some of the cost; and full, if the health insurance plan covered almost all to all of the cost. During the time of the study period (2003–2005), prescription drug coverage through the Medicare Part D program was not yet available.

Statistical Analysis

Multivariate logistic regressions were used to examine the independent effect of adjuvant HT modality on the probability of experiencing financial difficulty, controlling for prescription drug coverage, income, and the array of patient's socio-demographic characteristics defined above. A similar approach was used to examine the effects of drug coverage, income and other socioeconomic factors on the probability of switching adjuvant HT modality (primarily from TX to an AI) over the study period.

We tested the sensitivity of our findings by examining several variants of the model (e.g., by including square terms to capture possible nonlinearities or interaction terms between certain characteristics of interest). Our findings were remarkably robust to these alternative specifications, none of which yielded improved model fit.

Based on parameters estimates from these logistic regressions, we computed adjusted probabilities of experiencing

financial difficulty and of switching HT modality.[17] All statistical analyses were performed using STATA 10 statistical software (College Station, TX).

RESULTS

Sample Characteristics

A total of 3,038 women participated in the first wave of the survey. Of those, 96 were excluded because of missing values in variables related to use or timing of adjuvant HT. Of the remaining 2,942 respondents, 1,000 women reported no use of adjuvant hormonal therapy in the first 12 months post surgery; these observations were, therefore, excluded from the current analysis. An additional 52 women were excluded from our analysis due to missing information on one of our key variables—financial difficulty. This yielded a working sample of 1,890 breast cancer survivors who received HT in the first year post-incident breast cancer surgery. Table 1 shows the summary characteristics of the sample overall and by adjuvant hormonal therapy modality (TX only, AI only, or regimen switchers).

Among this cohort of elderly Medicare beneficiaries, a third was less than 70 years of age. The vast majority (90%) were white, most were either married (51%) or widowed (37%) and had a college degree (58%). Despite high levels of education, only about one-quarter had annual incomes above $45,000 and one out of every six women were at or below $15,000. With respect to drug coverage, nearly 80% reported having some insurance drug coverage (through Medicaid or private supplemental plans). The sample was relatively evenly split across the four states (Florida: 31.7%, Illinois: 21%, New York: 22.1%, California: 25.2%).

Summary statistics by adjuvant HT modality reveal differences across therapy groups by age, marital status, education and income. Most notably, compared to women who took only TX, women who received AI only or were switched during the study period tended to be younger, have a college degree and were less likely to lack drug coverage (Table 1).

Table 1. Sample Characteristics, Overall and by Adjuvant Hormonal Treatment Modality

Characteristics (%)	Overall	Adjuvant hormone treatment modality		
		AI only N=889	TX only N=652	Switched N=349
Age				
65–69	33.6	35.9	29.3	35.8
70–74	32.7	30.6	34.5	34.7
75–79	22.5	22.9	23.2	20.1
80+	11.2	10.6	13.0	9.4
Race/Ethnicity				
White	90.3	90.9	90.2	89.4
Black	3.2	2.8	2.9	4.6
Hispanic	3.8	4.0	3.5	3.7
Other	2.7	2.3	3.4	2.3
Marital status				
Married	50.7	51.9	47.8	53.3
Divorced	8.6	8.7	8.1	9.2
Widowed	36.6	35.1	40.3	33.5
Never married	4.1	4.3	3.8	4.0
Education				
Less than HS	7.6	6.9	8.7	7.7
High School	34.7	32.5	36.7	36.4
College	57.7	60.6	54.6	55.9
Comorbidities				
None	68.6	67.9	69.5	68.2
1 or more	31.4	32.1	30.5	31.8
Annual household income				
Less than $15,000	15.8	14.8	17.9	14.9
15,000–29,999	28.7	30.1	29.3	24.1
30,000–44,999	14.4	13.3	14.4	17.5
45,000+	23.0	24.3	20.8	23.2
Missing income information	18.1	17.5	17.6	20.3
Drug coverage				
None	17.6	15.1	21.8	16.0
Partial	35.8	37.0	35.6	33.2
Full	45.0	46.1	41.5	48.8

Factors Associated with Experience of Financial Difficulty Among Breast Cancer Survivors

Women who had taken only AI were more likely to experience financial difficulty than women who took only TX (OR=1.4; 95% CI: 1.1–1.7, Table 2). Compared to users of TX only, there was no difference in the odds of experiencing financial difficulty among women who switched between TX and AI. Breast cancer survivors with no drug coverage (OR=4.5; 95% CI: 3.3–5.9) or partial drug coverage (OR=3.6; 95% CI: 2.8–4.5) were more likely to experience financial difficulty compared to those with full coverage.

Widowed women were less likely than married breast cancer survivors to experience financial difficulty. Being divorced or never married, on the other hand, did not increase a woman's likelihood of experiencing financial difficulty relative to her married counterparts. Household income was a significant predictor of experiencing financial difficulty. Relative to women in the highest income bracket (those with annual household income at or above $45,000), women with lower incomes were more likely to experience financial difficulties. Once income was controlled for, educational attainment was not correlated with financial difficulty.

To put the results into perspective, we computed the probabilities that a woman with certain characteristics (e.g., taking AIs only or with no drug coverage) would experience financial difficulty, when controlling for all the other factors in the model. For women taking TX alone, the adjusted probability was 31%. This probability increased to 34.5% among switchers and to 37.1% among those using AI only. These differences represent the independent effect of HT modality on financial difficulty, after controlling for income, drug coverage, and other confounding variables described above. Differences were even more marked for drug coverage. Patients with full coverage had only a 20% adjusted probability of experiencing financial difficulty, compared to 45% among those with partial and 51% among those with no coverage.

Table 2. Correlates of Experiencing Financial Difficulties and Switching Adjuvant HT Modalities

Outcome	Experiencing financial difficulties		Switching adjuvant HT modality	
	Odds ratio	95% CI	Odds ratio	95% CI
Treatment modality				
AI only	1.4*	1.1–1.7		
Switched modality	1.2	0.9–1.7		
TX only	Reference	Reference		
Drug cost coverage				
None	4.5*	3.3–5.9	0.7*	0.5–0.9
Partial	3.6*	2.8–4.5	0.8	0.6–1.0
Full	Reference	Reference	Reference	Reference
Race/Ethnicity				
Black	0.9	0.5–1.8	1.6	0.9–3.0
Hispanic	1.2	0.8–2.2	1.1	0.6–1.6
Non-black, non-Hispanic	Reference	Reference	Reference	Reference
Marital status				
Married	Reference	Reference	Reference	Reference
Divorced	1.1	0.8–1.7	1.1	0.7–1.8
Widowed	0.6*	0.5–0.8	0.9	0.7–1.2
Never married	0.7	0.4–1.1	1.1	0.5–1.9
Education				
Less than HS	Reference	Reference	Reference	Reference
High school	1.0	0.6–1.4	1.4	0.8–2.2
College	0.9	0.6–1.3	1.2	0.8–2.0
Income				
Less than 15,000	1.7*	1.1–2.8	0.9	0.5–1.5
15,000–29,999	3.1*	2.3–4.3	0.6*	0.4–0.9
30,000–44,999	1.8*	1.3–2.5	0.8	0.6–1.2
45,000+	Reference	Reference	1.1	Reference
Missing information	0.8	0.5–1.4	1.4	0.6–1.1

***Note**: Both outcomes were estimated using a Logit model. In addition to the variables shown above, both regressions included indicators of age group, comorbid conditions, state of residence, and a constant term. Statistically significantly differences at the p<0.05 level are indicated by an asterisk.*

Factors Associated with Switching Adjuvant HT Modality

Drug coverage was the main factor associated with the likelihood of switching adjuvant HT modalities (Table 2). Women with no drug coverage had only a 14% adjusted probability of switching therapy from TX to an AI (OR=0.7; 95% CI: 0.5–0.9) compared to 33% of women with partial and 50% of women with full coverage. Women near poverty (i.e., those with annual household income between $15,000–$29,999) were less likely than wealthier BC survivors to switch regimens (OR=0.6; 95% CI: 0.4–0.9). However, the likelihood of switching HT modality over the study period was not significantly correlated with other socio-demographic, economic or geographic factors.

DISCUSSION

Increasingly, breast cancer is a chronic, controllable illness. Although there is a growing literature on the economics of cancer care, it has largely focused on the increasing proportion of global health spending accounted for by cancer care.[18–21] Little attention has been paid to the economic consequences of cancer among survivors and their families.

We found that patients who were treated solely with the more expensive AI drugs were more likely to experience financial difficulties. Not surprisingly, insurance drug coverage and financial status were also important factors. Women with full drug cost coverage and higher income levels were less likely to experience financial difficulties than those with partial or no drug coverage or less income. These findings are consistent with results from a recent survey conducted by the USA Today, Kaiser Family Foundation, and the Harvard School of Public Health, where it was reported that 33% of breast cancer patients have trouble paying for medical bills and 43% report skipping treatments or not filling prescriptions because of the cost [22].

Our study differs from previous work in three important respects. First, its focus is on a large, population-based sample of elderly women with incident breast cancer. Second, our focus is on prescription drug outlays which, as opposed to medical care costs, are often not (or only partially so) covered by insurance plans. Finally, we explicitly address the economic burden of newer, costly adjuvant hormone therapy regimes, controlling for SES and a wide array of potential confounders.

The cost difference between TX and AIs, even among those with some drug coverage, may influence a women's choice of which adjuvant HT option to pursue. Previous studies of women of lower socioeconomic status have consistently shown worse survival from breast cancer that women of higher socioeconomic status. [23,24] While there are numerous important potential confounding variables that contribute to this difference, one possibility is cost of outpatient medications. Although TX is currently generic, it is plausible that the previously higher expense of this drug may have contributed to this discrepancy. Unfortunately, few population-based data on use of hormonal therapies exist dating to that time.

Our results highlight the critical role of drug coverage in reducing financial hardship due to breast cancer treatment. In this study, even women with partial drug coverage had significantly higher odds of experiencing financial difficulty. This has important policy implications since, in addition to high premiums and co-pays, the recently enacted Medicare Part D program has strict annual coverage limits. In fact, a recent Kaiser Family Foundation study found that one in four Part D enrollees in 2007 reached their coverage gap.[25] Our results suggests that absence of full drug coverage is a major deterrent for use of the more effective, yet more expensive, AI treatment. These findings are consistent with reports that patients tend to change their use of prescription drugs when required to pay the full cost of medications in the coverage gap, either by stopping the drug therapy, switching to another medication in the class, or reducing the number of drugs they are taking.[25] The prospect of reaching the "doughnut hole" combined with analysts' forecast of a dramatic increase in the cost of Medicare Part D premiums in 2009 and years ahead for the most commonly used plans [26] raises fear that more breast cancer survivors will find themselves with less than full coverage for the AI agents after the Plan's enactment than before. This is particularly concerning given evidence that one in five breast cancer patients with insurance use up all or most of their savings during the course of treatment.[13]

Enhanced drug coverage has the potential to promote the use of more effective, guideline-based adjuvant HTs and to reduce impoverishment secondary to breast cancer treatment. It remains to be seen the extent to which that promise will be realized for elderly breast cancer survivors.

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