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Prescription Drug Coverage: Implications for hormonal therapy adherence in women diagnosed with breast cancer

Cathy J. Bradley, PhD. [Associate Director],

Population Sciences, University of Colorado Comprehensive Cancer Center, Professor, Department of Health Systems, Management, and Policy, School of Public Health, University of Colorado, Mailing Address: MS F-434, Physical Address: Bldg. 500, 6th Floor, C6004, 13001 E. 17th Pl., Aurora, CO 80045

Bassam Dahman, PhD. [Assistant Professor],

Department of Health Behavior and Policy, School of Medicine, Virginia Commonwealth University, Richmond, VA

Reshma Jagsi, MD.,

Department of Radiation Oncology, School of Medicine, University of Michigan, Ann Arbor, MI 48109

Steven Katz, MD., and

Department of Internal Medicine, Division of General Medicine, University of Medicine, University of Michigan, Ann Arbor, MI 48109

Sarah Hawley, PhD.

Division of General Medicine, School of Medicine, University of Medicine, University of Michigan, Ann Arbor, MI 48109

Cathy J. Bradley: cathy.bradley@ucdenver.edu; Bassam Dahman: Bassam.Dahman@vcuhealth.org; Reshma Jagsi: rjagsi@umich.edu; Steven Katz: skatz@umich.edu; Sarah Hawley: sarahawl@med.umich.edu

Abstract

Purpose—In spite of its demonstrated benefits, many women do not initiate hormonal therapy, and among those who do, many discontinue it prematurely. We examined determine whether differences in hormonal therapy adherence may be at least partially explained by the availability of prescription drug coverage.

Methods—Women aged 20 to 79 years diagnosed with stage 0-III breast cancer between June 2005 and February 2007 were enrolled in the study. Women completed a mailed survey, on average nine months after diagnosis, and again approximately four years later (N=712). Adjusted logistic regression was used to predict the likelihood of initiating hormonal therapy and hormonal therapy continuation.

Conflict of Interest Statement

None of the authors have any potential conflicts of interest to disclose.

All authors had full access to the data and participated in the design, analysis, and interpretation of the data. Bradley was responsible for drafting the manuscript. All authors reviewed the manuscript before submission.

Results—Women who had prescription drug coverage were more likely to initiate hormonal therapy relative to women without prescription drug coverage (OR=2.91, 95% CI=1.24 to 6.84). Women with prescription drug coverage were also more likely to continue hormonal therapy (OR=2.23; 95% CI=0.99 to 5.05, $p=0.0543$). The lowest income women were also less likely to continue hormonal therapy relative to women with annual household income that exceeded \$70,000 (OR=0.55; 95% CI=0.29 to 1.04) with a borderline significance of ($p=0.08$).

Conclusion—This study demonstrates the critical role of prescription drug coverage in hormonal therapy initiation and continuation, independent of health insurance coverage. These findings add to the body of literature that addresses medication adherence. Financial factors must be considered along with behavioral factors that influence adherence, which is becoming increasingly relevant to oncology as treatments are shifted to oral medications, many of which are very expensive.

Keywords

hormonal therapy adherence; prescription drug coverage; health insurance

Introduction

Hormonal (endocrine) therapy is an important component of hormone-receptor positive breast cancer treatment. Adherence to hormonal therapy recommendations is shown to prevent breast cancer recurrence and improve survival [1–4]. These medications can result in a 50% reduction in breast cancer recurrence in women at high risk for recurrence [5]. However, in spite of its demonstrated benefits, many women do not initiate hormonal therapy, and among those who do, many discontinue it before the full 5 to 10 years recommended following surgery for breast cancer [6–9].

Women who fail to initiate hormonal therapy or discontinue it prematurely are at considerably greater risk for recurrence than women who follow prescribed guidelines. Reasons for failing to initiate or discontinue hormonal therapy include side effects such as fatigue, hot flashes, vaginal dryness or discharge, and mood swings [6]. However, non-adherence to hormonal therapy recommendations is also associated with factors such as age [10], race, socioeconomic status, and health insurance [7, 10–13].

How health insurance and specifically, prescription drug coverage, influences hormonal therapy adherence is unclear. For example, some studies indicate that Medicaid insurance, which usually has generous prescription drug coverage, increases the likelihood of hormonal therapy initiation [10]; other studies have shown a negative relationship between Medicaid and hormonal therapy adherence [11]. Uninsured women's patterns of adherence are unknown, although studies of outcomes including recurrence and survival among uninsured women indicate generally unfavorable trends [14]. We hypothesize that differences in hormonal therapy adherence may be at least partially explained by the availability of prescription drug coverage. We focus on prescription drug coverage as opposed to health insurance in general since plans vary in prescription drug benefits. Findings from this study have important implications given the vigorous debates at a national level about health

insurance benefits and prescription drug coverage [15] balanced against concerns about drug costs and adherence to potentially lifesaving therapies.

Study population

This study was part of a larger study conducted on a longitudinal cohort of women diagnosed with breast cancer in metropolitan Los Angeles and Detroit. Women aged 20 to 79 years diagnosed with stage 0-III breast cancer between June 2005 and February 2007, as reported to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) population-based program registries in those regions were identified and approached for study participation. Methods for sample selection and data collection are published elsewhere [16–19]. Women completed a mailed survey, on average nine months after diagnosis, and again approximately four years later. Responses to the baseline and follow-up surveys were combined into a single dataset, into which clinical data from SEER was merged.

A total of 1536 women completed both surveys. In order to select a sample appropriate to study hormonal therapy use, we excluded women who were not eligible for hormonal therapy. These women had invasive disease ($n=381$), had negative or unknown ER and/or PR receptor status ($n=307$), or had experienced a recurrence ($n=41$). We also excluded women who had incomplete data on prescription drug coverage ($N=11$) and a handful of women with missing data on demographic information ($N=10$), leaving 712 women in the analytic sample.

Hormonal therapy and prescription drug coverage

The outcome variables were initiated hormonal therapy and hormonal therapy continuation at the second interview. Women were considered to have initiated hormonal therapy if they responded affirmatively to either of these follow-up interview questions: “Have you taken any of the following hormonal breast cancer medicines in the past week: Exemestane (Aromasin); Letrozole (Femara); Tamoxifen (Nolvadex); Anastrozole (Arimidex)?” or “Have you ever taken any of the following hormonal breast cancer medicine such as Exemestane (Aromasin), Letrozole (Femara), Tamoxifen (Nolvadex), or Anastrozole (Arimidex)?” Among those women who initiated hormonal therapy, those who responded “yes” to having taken hormonal breast cancer medicines in the past week were considered as continuing hormonal therapy at the second interview. We recorded whether patients had prescription drug coverage as a dichotomous variable.

Control variables

Patient demographic variables were also included in the analysis. Race/ethnicity was categorized as White, African American, Latina/Spanish-speaking, Latina/English-speaking or other. Age at the time of diagnosis was entered into the model as a continuous variable. We controlled for education (less than a high school degree, high school diploma or GED, some college or technical school, college graduate), marital status (married/partnered or divorced, separated, or widowed, and never married), employment status (working or not working), annual household income (less than \$40,000, \$40,000 to \$69,999, and greater than

\$70,000 or missing), cancer stage (I, II, or III). We also included whether women were identified from the Los Angeles or the Detroit SEER registries.

Statistical Analysis

The sample characteristics were analyzed descriptively by whether the woman reported having prescription drug coverage at the follow-up survey. Statistically significant differences in the means of continuous normally distributed variables were tested using *t*-tests. Statistical significance of categorical differences (e.g., race, education, marital, employment status) between women with and without prescription drug coverage was determined using Chi-square tests.

We estimated adjusted logistic regression models to measure the relationship between pre-specified independent variables of prescription drug coverage, patient demographic characteristics, cancer stage, and hormonal therapy initiation and continuation. Because having health insurance is positively correlated with having prescription drug coverage, we estimated two sets of models, one that included insurance coverage and another that excluded health insurance coverage. We use self-reported insurance status reported at the first and second interview to create a variable that reflected whether women remained continuously insured (either publicly or privately insured or other), changed insurance status (gaining insurance, changing from private to public or public to private), or became uninsured and remained so at the time of the second interview. We do not capture periods of uninsurance or a change in a specific policy, but instead have information on the general category of health insurance coverage (public including Medicaid and Medicare, private whether through an employer or purchased policy, a small number of other, and uninsured). The estimated odds ratios were virtually unchanged with the addition of these variables (results not shown). Therefore, we report only the results from parsimonious models. We report odds ratios (OR) and 95% confidence intervals (CI). All analyses were conducted using SAS, version 9.4 and were weighted using survey procedures to account for differential probabilities of sampling and non-response. The study was approved by Institutional Review Boards at the University of Michigan, University of Southern California, and Wayne State University.

Results

Table 1 reports the sample characteristics by whether women had prescription drug coverage. A higher percentage of women with prescription drug coverage initiated and more women continued hormonal therapy at the time of the second interview. Nearly all women with prescription drug coverage initiated hormonal therapy (90%). At the time of the second survey (approximately 4 years later), 81% of women with prescription drug coverage were still taking hormonal therapy whereas only 66% of the women without prescription drug coverage continued taking hormonal therapy.

Table 2 reports results from adjusted logistic regression models that predict the likelihood of initiating and discontinuing hormonal therapy. Women who had prescription drug coverage were more likely to initiate hormonal therapy relative to women without prescription drug

coverage (OR=2.91, 95% CI=1.24 to 6.84). Women with prescription drug coverage were also more likely to continue hormonal therapy (OR=2.23; 95% CI=0.99 to 5.05, $p=0.0543$).

Annual household income was also found to be associated with hormonal therapy initiation. Women with an annual household income below \$40,000 were much less likely to initiate hormonal therapy (OR=0.39; 95% CI 0.18, 0.83). Likewise, the lowest income women were less likely to continue hormonal therapy relative to women with annual household income that exceeded \$70,000 (OR=0.55; 95% CI=0.29 to 1.04) with a borderline significance of ($p=0.08$).

English-speaking Latinas were more likely to initiate therapy than white patients (OR=2.39, 95% CI 1.10 to 5.19). However, this difference was not significant when adjusted for the multiple testing of pairwise comparisons between all racial and ethnic groups.

Conclusions

We found a strong positive relationship between hormonal therapy initiation and prescription drug coverage. A similar relationship was observed for hormonal therapy continuation. Emerging evidence indicates that the out-of-pocket costs of cancer treatment impose a significant burden on cancer patients [20]. A prior published study further suggested that higher prescription drug co-payments are associated with hormonal therapy non-compliance [21]. We add to this literature by jointly examining patient characteristics, health insurance coverage, and prescription drug coverage in a racially diverse sample drawn from a population-based registry. Studies of low-income uninsured and Medicaid insured women are often drawn from teaching hospitals or safety net settings [22] whereas studies of prescription drug coverage are drawn from claims data of privately insured individuals where the effect of having private insurance, which can greatly reduce total financial burden, cannot be disentangled from the prescription drug benefit. The present analysis overcomes these limitations.

The number of oral medications used in oncology is rapidly increasing, making issues regarding adherence and compliance all the more relevant. This study adds to the body of literature addressing these topics in two ways. Our results demonstrate that prescription drug coverage plays an important role in hormonal therapy initiation and continuation. Moreover, our findings suggest that the prescription drug benefit has an influence on hormonal therapy initiation and continuation, independent of health insurance coverage. Therefore, prescription drug benefits factor into medication adherence, even among insured populations.

Nationally, coverage for prescription medications is the subject of robust debate. The Affordable Care Act (ACA) is gradually lowering the out-of-pocket costs for prescription drugs by offering subsidies to low-income adults and other subsidies that reduce beneficiary coinsurance [23]. Similarly, other ACA provisions such as those to limit cost sharing and out-of-pocket costs may also be important in reducing costs incurred by insured individuals. Given the findings of the current study, these changes may ultimately increase compliance with hormonal therapy recommendations for breast cancer patients.

Our study has a number of strengths including a sample drawn from a population-based registry, inclusion of uninsured women, racial and ethnic diversity, and its long-term follow-up period. The study has limitations as well. First, the data are self-reported. We did not have information from medical records or prescription drug claims to verify whether women complied with recommendations. Second, we do not have information on the amount of co-payments women were required to pay for hormonal therapy. Third, the study sample, although population-based, was drawn from the Detroit and Los Angeles metropolitan areas and therefore the results may not be generalizable.

In summary, this study demonstrates the critical role of prescription drug coverage in hormonal therapy initiation and continuation, independent of health insurance coverage. These findings add to the body of literature that addresses medication adherence. Financial factors must be considered along with behavioral factors that influence adherence, which is becoming increasingly relevant to oncology as treatments are shifted to oral medications, many of which are very expensive. The current study suggests that reluctance to insure prescription drugs may result in increased recurrence and poor survival among women with breast cancer, one of the largest groups of cancer survivors.

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Table 1

Descriptive statistics by prescription drug coverage (N=712)

Prescription Drug Coverage					No Prescription Drug Coverage	Total N
Total N	673		39		712	
Hormonal therapy						
Initiation**	606	90.04	32	82.05	638	
Discontinued**	117	19.31#	11	34.38#	128	
Continued**	489	80.69#	21	65.62#	510	
Age, Mean (SD)	673	57.67 (11.40)	39	57.44 (10.81)	57.66 (11.37)	
Race/ethnicity						
Latina, Spanish speaking	78	11.59	3	7.69	81	
Latina, English speaking	94	13.97	2	5.13	96	
Black	118	17.53	9	23.08	127	
White	376	55.87	22	56.41	398	
Other	7	1.04	3	7.69	10	
Education						
Less than a high school degree	106	15.75	3	7.69	109	
High school graduate or G.E.D	131	19.47	13	33.33	144	
Some college or technical school	230	34.18	16	41.03	246	
College graduate	206	30.61	7	17.95	213	
Marital Status*						
Married/partnered	407	60.48	21	53.85	428	
Not married/partnered	266	39.52	18	46.15	284	
Employment status						
Not working	279	41.46	21	53.85	300	
Working	394	58.54	18	46.15	412	
Annual household income**						
Less than \$40,000	208	30.91	19	48.72	227	
\$40,000 to \$69,999	131	19.47	8	20.51	139	

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	Prescription Drug Coverage		No Prescription Drug Coverage		Total N
Greater than \$70,000	221	32.84	3	7.69	224
Do not know/Refused/Missing	113	16.79	9	23.08	122
Location					
Los Angeles	366	54.38	18	46.15	384
Detroit	307	45.62	21	53.85	328
Cancer stage					
Stage I	354	52.60	20	51.28	374
Stage II	235	34.92	16	41.03	251
Stage III	84	12.48	3	7.69	87

Notes: Chi-square test for statistically significantly categorical differences from having prescription drug coverage at

** p<.05,
*** p<.01.
^a Percentage is estimated from those who initiated hormonal therapy.

Table 2

Multivariable models of hormonal therapy initiation and continuation, OR and 95% C.I.

	Initiation	Continuation
N	712	638 ^d
Prescription drug coverage		
Yes	2.91(1.24, 6.84) ^{**}	2.23(0.99, 5.05) [*]
No	Reference	Reference
Age	0.98(0.95, 1.00) [*]	1.00(0.98, 1.02)
Race		
Latina, Spanish speaking	1.75(0.73, 4.20)	1.03(0.49, 2.16)
Latina, English speaking	2.39(1.10, 5.19) ^{**}	1.47(0.79, 2.71)
Black	1.65(0.76, 3.56)	0.68(0.39, 1.19)
Other	7.15(0.35, 144.35)	1.42(0.29, 7.06)
White	Reference	Reference
Education		
Less than a high school degree	0.75(0.32, 1.75)	0.82(0.38, 1.75)
High school graduate	2.14(0.91, 5.06) [*]	0.68(0.36, 1.28)
Some college	0.89(0.47, 1.67)	0.76(0.44, 1.32)
College graduate	Reference	Reference
Marital status		
Not married or partnered	1.33(0.78, 2.28)	0.72(0.46, 1.12)
Married/partnered	Reference	Reference
Employment		
Working	0.88(0.51, 1.53)	1.12(0.71, 1.76)
Not working	Reference	Reference
Location		
Los Angeles	0.92(0.50, 1.69)	0.99(0.60, 1.65)
Detroit	Reference	Reference
Cancer Stage		
II	1.04(0.63, 1.72)	1.1(0.73, 1.67)
III	1.58(0.71, 3.51)	2.22(1.12, 4.4) ^{**}
I	Reference	Reference
Household income		
Less than \$40, 000	0.39(0.18, 0.83) ^{**}	0.55(0.29, 1.04) [*]
\$40, 000 to \$69, 999	1.12(0.49, 2.56)	0.73(0.39, 1.38)
Do not know/Refused/Missing	0.60(0.27, 1.30)	0.57(0.29, 1.11) [*]
Greater than \$70, 000	Reference	Reference

Notes: OR=odds ratio; CI=Confidence Interval. Statistically significant

^{*}
p<.10^{**}
p<.05;

p<.01.

& Sample excludes 74 women who did not initiate hormonal therapy.

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