Effects of Breast Cancer on Chronic Disease Medication

Adherence Among Older Women

Running Head: Breast Cancer and Chronic Disease Medication Adherence

Melissa L. Santorelli¹, Michael B. Steinberg², Kim M. Hirshfield^{2,3}, George G. Rhoads¹

Elisa V. Bandera^{1,2,3}, Yong Lin⁴, Kitaw Demissie^{1,3}

Rutgers, The State University of New Jersey

¹School of Public Health, Department of Epidemiology

²Rutgers Robert Wood Johnson Medical School

³Rutgers Cancer Institute of New Jersey

⁴School of Public Health, Department of Biostatistics

Corresponding Author: Melissa L. Santorelli

683 Hoes Lane West, Piscataway, NJ 08854

Email: veziname@sph.rutgers.edu, Phone: 732-267-4409, Fax: 732-235-5418

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ABSTRACT

PURPOSE

The purpose of this study was to determine the effects of breast cancer on chronic disease medication adherence among older women.

METHODS

The Surveillance, Epidemiology and End Results (SEER) - Medicare linked data and a 5% random sample of Medicare enrollees were used. Stage I-III breast cancer patients diagnosed in 2008 and women without cancer were eligible. Three cohorts of medication users 66+ years were identified using diagnosis codes and prescription fill records: diabetes, hypertension and lipid disorders. For each cohort, breast cancer patients were frequency matched to comparison women by age and geographic area. Medication adherence was measured by the proportion of days covered (PDC) and medication persistence.

RESULTS

During the post-baseline period, the percentage of breast cancer patients who were non-adherent was 26.2% for diabetes medication, 28.9% for lipid lowering medication, and 14.2% for hypertension medication. Breast cancer patients experienced an increased

odds of diabetes medication non-adherence [Odds Ratio (OR) = 1.44; 95% Confidence Interval (CI) = 1.07 to 1.95] and were more likely to be non-persistent with diabetes medication [Hazard Ratio = 1.31; 95% CI: 1.04 to 1.66] relative to women without cancer. The study failed to show a difference between breast cancer and comparison women in the odds of non-adherence to hypertensive (OR=0.87; 95% CI: 0.71 to 1.05) or lipid lowering medication (OR=0.91; 95% CI: 0.73 to 1.13) with a PDC threshold of 80%.

CONCLUSION

Special attention should be given to the coordination of primary care for older breast cancer patients with diabetes.

INTRODUCTION

Improving survival has raised important questions about the long term health of breast cancer patients. Understanding the effects of breast cancer on chronic disease medication adherence among older women is essential because the majority of these patients will die of causes other than their breast cancer.¹ Older women are also of special interest because they experience the highest incidence of breast cancer² and are likely to have other chronic conditions that require medication use. Among older adults in the United States, approximately 61% have at least two chronic conditions and approximately 76% are taking at least two medications.^{3,4} This suggests that many older women with breast cancer will be taking chronic disease medications, including those that are known to control diabetes and prevent cardiovascular events.

Although not specific to breast cancer patients, a strong relationship between chronic disease medication adherence and positive health outcomes has been established in general populations. A retrospective study of thirteen health plans showed that hypertensive patients with high levels of medication adherence were 45% more likely to achieve blood pressure control after adjusting for age, gender, and comorbidity.⁵ Similarly, a large retrospective cohort study of patients with coronary artery disease revealed a significant association between adherence with prescribed cardiovascular disease medications and reduced mortality, both all-cause and cardiovascular disease related.⁶ Adherence with diabetes medications has also been associated with positive health outcomes such as lower hospitalization and mortality rates.^{7,8}

Two previous studies documented a decrease in the proportion of patients who were adherent with chronic disease medication in relation to breast cancer diagnosis, but comparison groups were not used and so these studies could not distinguish observed changes from ordinary declines that would occur over time.^{9,10} Therefore, the true effects of breast cancer on chronic disease medication adherence remain unknown. Women with breast cancer are likely overwhelmed with the competing demands of cancer treatment and may therefore be less likely to self-manage chronic health conditions or to follow up with other specialists. Cancer treatments may also interact with chronic disease medications consequently modifying their tolerability. Furthermore, medical oncologists may not address primary care issues like chronic disease medication use, unless they interfere with cancer treatment.

The objective of this study was to evaluate the effects of breast cancer diagnosis on diabetes, lipid lowering, and hypertension medication adherence.

METHODS

Setting

A retrospective cohort study was conducted using data from the Surveillance, Epidemiology, and End Results (SEER) – Medicare linked data files. This study was approved by the Rutgers New Brunswick Health Sciences IRB.

SEER Registries Data

The SEER registries capture incident cancer for approximately 28% of the United States¹¹ and serve as a recognized population based source for information about

cancer cases. The National Cancer Institute oversees the SEER program and maintains high standards for quality control and quality improvement.¹²

Medicare Data

Approximately 93% of SEER records, for patients 65 years and older, have been linked with Medicare enrollment records.¹³ Medicare provides federal health insurance with eligibility for non-disabled adults occurring at 65 years of age. About 97% of older adults in the United States are enrolled in Part A, which includes coverage for hospitalizations. About 96% of older adults who are enrolled in Part A pay the premium to enroll in Part B, which includes coverage for physician services and other outpatient care.¹³ Since July 2006, prescription coverage has been available to beneficiaries through Medicare Part D and in 2008, 53.4% of SEER-Medicare linked patients with breast cancer were enrolled in this program.¹⁴

Study Population

The study population included women with stage I-III breast cancer (AJCC 6th edition) who were diagnosed in 2008 at age 66 years or older and comparison women without cancer who were alive on a randomly assigned date during the same year (Supplementary Figure S1).

Breast Cancer Patients

Breast cancer patients without a previous cancer history were assessed for eligibility except when the source of cancer diagnosis was noted as autopsy or death certificate. Continuous fee-for-service enrollment in Part A, Part B, and Part D coverage

was required during the year before cancer diagnosis and for two years after. Patients who died within two years following their cancer diagnosis were not eligible. Enrollment into the diabetes, lipid disorders, and hypertension cohorts required a corresponding diagnosis to be listed on at least two different outpatient claims, more than thirty days apart, during the year prior to breast cancer diagnosis (Supplementary Table S1). Patients with diabetes were not eligible for the hypertension and lipid disorders cohorts. Diabetic patients are treated more aggressively for hypertension and blood pressure control is defined using a more conservative threshold.¹⁵ According to the American Diabetes Association, control of hypertension is vital to preventing diabetes complications.¹⁶ Therefore, adherence to hypertension medication may be seen as one of the many components involved in diabetes self-management and adherence to lipid lowering medication may be viewed in a similar manner. For these reasons, we aimed to study the effects of breast cancer on hypertension and lipid lowering medication adherence only among patients without diabetes.

In addition to meeting diagnosis criteria, eligible patients must have filled at least two prescriptions for at least one relevant medication class during the year prior to breast cancer diagnosis and must have had at least a one day supply of medication available on the date of breast cancer diagnosis. Relevant medication was defined as any oral diabetes class for the diabetes cohort, any hypertension class for the hypertension cohort, and as the HMG-CoA reductase inhibitor (statin) class for the lipid disorders cohort (Supplementary Table S2). Other classes of lipid lowering medication

were not considered in the selection of patients since statins are the most effective and widely used, with fewer side effects, when compared to other agents¹⁷. Patients who filled prescriptions for insulin in the year before breast cancer diagnosis or during the two years following were excluded from all three cohorts because there are no known methods to capture adherence with injected medications using prescription fill records.¹⁸ Patients who were hospitalized during the year prior to diagnosis were also excluded as these women likely received their medication from a hospital pharmacy for a period of time making it difficult to determine eligibility according to prescription fill records.

The final diabetes cohort included 298 women with breast cancer (54.0% stage I, 26.5% stage IIA, 8.7% stage IIB, 10.7% stage III). The lipid disorders cohort included 508 women with breast cancer (63.4% stage I, 20.3% stage IIA, 9.7% stage IIB, 6.7% stage III) and the hypertension cohort included 1,062 women with breast cancer (61.6% stage I, 22.7% stage IIA, 8.4% stage IIB, 7.3% stage III).

Comparison Women

Comparison women were selected from a 5% random sample of Medicare enrollees living in areas served by the SEER cancer registries. Beneficiaries from this sample who appeared in the SEER registries as a cancer case were not included. Women who were alive at the end of 2007 were randomly assigned a mock cancer diagnosis date from January 1, 2008 to December 31, 2008 and beneficiaries who were 66 years of age or older on the assigned date were assessed for eligibility. Comparison women who met all selection and cohort enrollment criteria were frequency matched to

breast cancer patients by age and geographic area of residence using four times as many comparison patients as there were breast cancer patients in each stratum.

Outcomes

Part D prescription events were reviewed for two years following the date of diagnosis. Prescription fill dates and amount dispensed during this period were used to calculate the proportion of days covered (PDC) and medication persistence. Although patients in the lipid disorders cohort were selected based on their use of statins only, prescriptions for other lipid lowering medication (cholesterol absorption inhibitors, nicotinic acid derivatives, bile acid sequestrants, fibric acid derivatives) were also monitored in order to account for patients who might have switched to other types of medication.¹⁷

Proportion of Days Covered

For each patient in a given cohort, the proportion of days covered (PDC) during the year prior to baseline (pre-baseline) and during the two year measurement period (post-baseline) was calculated. The PDC approach uses fill dates and days supplied for each dispensed prescription in order to create coverage indicator variables for each day.^{19,20} Separate coverage indicator variables were created for each medication class and patients who were taking medication from more than one class were considered adherent on a given day if they were covered by at least one.²¹ Baseline medication supply was carried over when creating the class specific coverage indicator variables for the post-baseline period and early refill dates were adjusted forward so that patients

could be credited with the entire amount that was dispensed with each fill.^{19,20} In order to calculate the PDC for each patient, the number of adherent days was added and this total was then divided by the number of days in the measurement period. Any periods of inpatient hospitalization were excluded from the denominator since medication was likely held appropriately or provided by a hospital pharmacy during these times. Consistent with the literature, patients were classified as non-adherent if they achieved a PDC of less than 80%.^{22,23} However, a sensitivity analysis was also performed by setting the threshold for non-adherence at 70% and 90%.

Medication Persistence

Medication persistence describes how long a patient continues to take medication after initially filling a prescription. Persistency was monitored for the first 18 months of the measurement period and the largest number of consecutive days without coverage by a relevant medication class was identified for each patient, with periods of hospitalization deducted from this number. For the diabetes and hypertension cohorts, non-persistence was defined as being without medication for 26 days and for the lipid lowering cohort, non-persistence was defined as being without medication for 62 days. In our group, exceeding these identified gaps in coverage during an 18 month follow up period had been shown to optimize sensitivity and specificity in predicting longer term discontinuation for older breast cancer patients (data available upon request). Patients that did not exceed the allowable gap in coverage were treated as censored.

Exposure

The main exposure variable indicated whether or not each woman had breast cancer.

Other Variables

Demographic variables included age, race, and geographic area of residence. Date of birth from the Medicare enrollment record was compared to the diagnosis date to calculate age, which was further categorized into groups (66-69 years, 70-74 years, 75-79 years, 80-84 years, 85+ years). Race was also based on the Medicare enrollment record and was categorized as white, black, or other. Geographic area of residence for each patient was determined by the designated SEER cancer registry. All of the California registries and both registries in Georgia were aggregated by state. An estimate of daily pill burden was calculated using all prescriptions filled during the year prior to baseline. Days of medication supplied were summed and this total was divided by the number of days that elapsed between first prescription fill date and coverage end date for the last prescription filled. Daily pill burden was treated as a continuous measure for the statistical analysis and then categorized after rounding to a whole number for descriptive purposes (≤ 2 , 3-4, or 5+ pills per day).

Statistical Analyses

For each cohort of chronic disease medication users, logistic regression was used to model the relationship between breast cancer diagnosis and non-adherence after adjusting for race, age, and daily pill burden. Separate models were used for each binary measure of non-adherence (PDC < 70%, PDC < 80%, PDC < 90%). Kaplan

Meier estimates were plotted comparing time to non-persistence for women with and without breast cancer and the log-rank test was used to compare distributions between the two groups. Cox proportional hazards models were used to estimate hazard ratios describing the effects of breast cancer diagnosis on non-persistence after adjusting for race, age, and daily pill burden. Generalized Estimating Equation (GEE) analyses was also used to estimate the relative change in non-adherence odds from the pre-baseline to the post-baseline period for breast cancer patients and comparison women in each cohort. An exchangeable working correlation structure was used for the GEE analyses to account for the lack of independence among observations.

RESULTS

As shown in Table 1, women of all age groups were represented reasonably well with the lowest representation found among women 85 years and older in each cohort. The racial distribution for each cohort showed that the percent of white patients was somewhat higher for women with breast cancer when compared to that of women without breast cancer. For the diabetes and hypertension cohorts, the proportion of patients who were non-adherent during the year prior to baseline was similar for women with and without breast cancer. For the lipid disorders cohort, the proportion of patients who were non-adherent during the year prior to baseline was somewhat higher for women with breast cancer when compared to women without breast cancer. During the post-baseline period, the percentage of breast cancer patients who were non-adherent

was 26.2% for diabetes medication, 28.9% for lipid lowering medication, and 14.2% for hypertension medication (Table 2).

Results from the logistic regression analysis are shown in Table 2. When non-adherence was defined as PDC < 80%, the odds of diabetes medication non-adherence was 44% higher for patients with breast cancer relative to patients without breast cancer after adjusting for age, race, and daily pill burden ($p=0.02$). When the non-adherence threshold for PDC was changed to 70% and 90% for diabetes medications, the effect was similar. In contrast, the odds of hypertension medication non-adherence was found to be 24% lower for patients with breast cancer when non-adherence was defined as PDC < 90% ($p<0.01$). However, a significant effect was not observed when the non-adherence threshold for the PDC was set at 70% or 80%. We failed to observe any differences between breast cancer and comparison patients in the odds of non-adherence with lipid lowering medication regardless of the non-adherence threshold.

Findings for non-persistence were consistent with those based on the PDC. Kaplan-Meier analysis shows the probability of non-persistence with diabetes medication was higher for women with breast cancer, when compared to women without breast cancer (Figure 1), while results in Figure 2 show the probability of non-persistence with hypertension medication was lower for women with breast cancer relative to comparison women. Kaplan-Meier analysis suggested similarity in lipid lowering medication non-persistence between both groups of women (Figure 3). Results from the Cox proportional hazards analysis (Table 3) show that women with breast cancer

experienced a 31% increase in the hazard for diabetes medication non-persistence relative to women without breast cancer after adjusting for age, race, and daily pill burden ($p=0.02$), while women with breast cancer experienced a 27% decrease in the hazard for hypertension medication non-persistence relative to women without breast cancer ($p<0.01$). We failed to observe a difference in non-persistence with lipid lowering medication between women with and without breast cancer.

In order to exclude the possibility that increased non-adherence with diabetes medication for breast cancer patients is explained by cancer treatment related effects, we performed a sensitivity analysis that looked at the association between breast cancer and non-adherence over varying periods of time within the two year measurement period. The results of this analysis are presented in Supplementary Table S3. The active treatment period for most breast cancer patients in our study would have been during the first six months following diagnosis. After excluding this period from the analysis, the odds of non-adherence ($PDC < 0.80\%$) remained 36% higher for breast cancer patients relative to comparison women (OR: 1.36; 95% CI: 1.01 – 1.83). The increased odds of non-adherence was 25% with borderline significance after excluding the first twelve months from the analysis (OR: 1.25; 95% CI: 0.93 – 1.68) and the increase was 15% and no longer significant after excluding the first eighteen months from the analysis (OR 1.15; 95% CI: 0.86 – 1.55). However, the odds remained consistently elevated for breast cancer patients by at least 25% with borderline significance during each time interval when the PDC threshold was set at 90%. We

performed the same sensitivity analysis for the hypertension cohort in order to determine whether better adherence with hypertension medication for breast cancer patients could be explained by increased exposure to the health care system during the active cancer treatment period. We found that the odds of non-adherence (PDC < 0.90%) remained 16% lower for breast cancer patients after excluding the first twelve months from the analysis (OR: 0.84; CI: 0.71 – 0.99), but this protective effect was no longer significant after excluding the first eighteen months from the analysis (OR: 0.90 95% CI: 0.76 – 1.06)

Relative changes in chronic disease medication non-adherence from the pre-baseline to the post-baseline period are shown in Table 4. The odds of non-adherence was higher in the post-baseline period relative to the pre-baseline period for both the breast cancer and comparison women in all three cohorts. When non-adherence was defined using a PDC threshold of 80%, the increase in non-adherence odds in the post-baseline period was 35% higher for breast cancer patients taking diabetes medication relative to comparison women taking diabetes medication. However, the difference between these groups did not achieve statistical significance ($p=0.09$). In contrast, the increase in non-adherence odds in the post-baseline period was 27% lower for breast cancer patients taking lipid lowering medication relative to comparison women taking lipid lowering medication and this difference was statistically significant ($p=0.02$). No detectable difference in the post-baseline increase in non-adherence odds between

breast cancer patients taking hypertension medication and comparison women taking hypertension medication was observed ($p=0.64$).

DISCUSSION

This study aimed to evaluate the effects of breast cancer diagnosis on chronic disease medication adherence among older women using a retrospective cohort design. Study results showed that women with breast cancer experienced a greater odds of non-adherence and a greater hazard for non-persistence with oral diabetes medication relative to a comparable group of women without breast cancer. Furthermore, the increase in non-adherence odds for diabetes medication from the pre-baseline to the post-baseline period for breast cancer patients was well beyond that which was observed for comparison women. These results are consistent with those of Calip and colleagues (2014), who reported a decline in the proportion of breast cancer patients who were adherent with diabetes medication both during and after breast cancer treatment. Their study also showed that among non-adherent women, the proportion with poor glycemic control increased during the same time period.¹⁰ The current study findings are also consistent with those from a small study of only 43 patients, which concluded that patients who were undergoing chemotherapy for cancer engaged in fewer diabetes self-management behaviors for reasons such as severity of symptoms and perceived prioritization of cancer by both patients and providers.²⁴ Our findings provide additional justification for interventions that reduce patient barriers and promote

diabetes medication adherence among breast cancer patients. In addition to the beneficial effects on diabetes outcomes, better adherence with diabetes medication may also have positive effects on cancer survival. Metformin, in particular, has been consistently associated with reduction in cancer recurrence and mortality.²⁵⁻²⁷

Another potential explanation for the negative association between breast cancer and diabetes medication adherence is that cancer treatments may interact with diabetes medications in a way that modifies their tolerability. For example, metformin is commonly taken for type II diabetes and this medication is known to have gastrointestinal side effects.^{28,29} Metformin may become less tolerable for diabetes patients who are receiving chemotherapy for breast cancer. It is also possible that some women lost weight, had hypoglycemia related to treatment or disease-related anorexia, nausea or vomiting, or were advised to discontinue their oral diabetes medication by their health care provider. Due to a limited sample size, the current study did not evaluate the role of cancer stage or cancer treatment so it is unclear whether the observed effects varied according to these factors. Our sensitivity analysis suggests that non-adherence persists even after the active treatment period ends, particularly when a conservative threshold is considered.

In contrast to findings for diabetes, breast cancer diagnosis was associated with improved adherence and improved persistence with hypertension medication. This could potentially be explained by differences in how conditions are monitored by providers. Oncologists may be more likely to follow up with breast cancer patients about their

hypertension when compared with other chronic conditions such as diabetes. Blood pressure readings are taken frequently in conjunction with routine care for breast cancer providing regular and recurrent opportunities to monitor hypertension control and to reinforce medication adherence. In contrast, glucose levels are not routinely monitored in oncology settings unless other blood tests in the same panel are relevant for cancer treatment. Our sensitivity analysis showed that the protective effect of breast cancer on hypertension medication adherence may no longer be apparent after eighteen months following diagnosis. This finding is consistent with the idea that better hypertension adherence among breast cancer patients may be attributed to increased exposure to the health care system.

It is important to note that this study did not account for changes in the need for chronic disease medication, which could be different for women with and without breast cancer. Calip, Boudreau, and Loggers showed in a relatively homogenous population that even though adherence with statins did not return to baseline after breast cancer diagnosis, LDL levels did return to baseline and they reasoned that this group of women could have been more likely to exercise or to improve their diet following breast cancer diagnosis.⁹ Some hormonal treatments for breast cancer have beneficial effects on lipid profiles and this could also reduce the need for lipid lowering medication among some breast cancer patients.³⁰⁻³² Our results regarding lipid lowering medication are difficult to interpret because unlike the other cohorts, the pre-baseline non-adherence measurement for lipid lowering medication among breast cancer patients (25.4%) was

high relative to that of comparison women (20.6%) suggesting that these groups were not comparable to each other at baseline.

This study has several other limitations. First, it included only Part D beneficiaries who have different characteristics when compared to Medicare recipients with other types of prescription coverage or to those without any prescription coverage.³³ For example, Part D enrollees are more likely to be disabled or to report fair/poor health when compared to others.^{33,34} It was also limited to those women with a documented diagnosis code for the conditions of interest so we likely missed some women who were taking chronic disease medication, but who did not have a corresponding diagnosis code documented because they did not seek medical care for their condition during the year prior to baseline. For this reason, our sample may be more representative of patients with newly diagnosed chronic conditions and of those with uncontrolled chronic conditions since these patients would be more likely to be seen for an office visit. Selection criteria also resulted in a study population that was relatively adherent during the year prior to baseline; therefore, generalizability of findings may be further limited. For example, the negative effects of breast cancer on diabetes medication adherence could be even larger in magnitude among less adherent populations. This study was also limited because patients taking medication in more than one class were considered adherent when covered by at least one of them. This approach can overestimate adherence and is not sensitive to whether or not patients adhere with all prescribed regimens. There is also potentially missing data as a result of the Medicare Part D

coverage gap between initial and catastrophic coverage limits when patients are forced to pay out of pocket, utilize drug assistance programs, or purchase medications through a generic retail prescription program.

The current study has several strengths that should be noted including a geographically diverse cohort. Most importantly, a comparison group was included to allow for the direct assessment of breast cancer effects on medication adherence unlike previous studies. The current study also included both PDC and persistence-based outcome measures. The PDC-based analysis tested effects across three different non-adherence thresholds instead of selecting a single cut-point for analysis and the thresholds that were used to define non-persistence had been previously shown to maximize sensitivity and specificity in predicting long term medication discontinuation in older breast cancer patients.

The findings from this study suggest that the effects of breast cancer on chronic disease medication adherence vary by type of chronic disease. While breast cancer has a negative effect on diabetes medication adherence, it seems to have a protective effect on hypertension medication adherence. Efforts to promote medication adherence among breast cancer patients with diabetes are necessary and learning more about facilitating factors that contribute to hypertension medication adherence among women with breast cancer may help to inform these efforts.

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FIGURE LEGENDS

Figure 1

Kaplan-Meier plots are showing diabetes medication persistence for women with and without breast cancer. Results from the log-rank test indicate a significant difference in the persistence of breast cancer and comparison women ($p=0.04$). The number of women at risk for non-persistence throughout the measurement period is also shown for both groups. The asterisk represents a value that has been suppressed to preserve patient confidentiality.

Figure 2

Kaplan-Meier plots are showing hypertension medication persistence for women with and without breast cancer. Results from the log-rank test indicate a significant difference in the persistence of breast cancer and comparison women ($p<0.01$). The number of women at risk for non-persistence throughout the measurement period is also shown for both groups.

Figure 2

Kaplan-Meier plots are showing lipid lowering medication persistence for women with and without breast cancer. Results from the log-rank test failed to show a significant difference in the persistence of breast cancer and comparison women ($p=0.95$). The number of women at risk for non-persistence throughout the measurement period is also shown for both groups.

SUPPLEMENTARY DATA

Supplementary Figure S1

Flow Diagram Showing Selection of Breast Cancer and Comparison Women

TABLES

Table 1 - Baseline Characteristics of the Study Population by Cohort

	Diabetes		Lipid Disorders		Hypertension	
	Breast Cancer	Comparison	Breast Cancer	Comparison	Breast Cancer	Comparison
	N = 298 %	N = 1,192 %	N = 508 %	N = 2,032 %	N = 1,062 %	N = 4,248 %
Age						
66-69	24.8	24.8	23.2	23.2	20.0	20.0
70-74	28.2	28.2	26.4	26.4	25.9	25.9
75-79	23.5	23.5	23.0	23.0	21.6	21.6
80-84	14.1	14.1	16.3	16.3	17.4	17.4
85 +	9.4	9.4	11.0	11.0	15.2	15.2
Race						
White	73.2	69.3	87.8	79.8	83.7	79.0
Black	12.4	13.4	5.7	6.4	8.8	7.6
Other ^a	14.4	17.3	6.5	13.8	7.5	13.4
Prior PDC^b						
≥ 80%	84.6	85.1	74.6	79.4	90.8	90.4

< 80%	15.4	14.9	25.4	20.6	9.2	9.6
Pill Burden^c						
≤ 2	9.4	10.0	24.2	20.8	28.0	23.8
3-4	32.2	33.1	40.4	39.5	41.8	41.5
5+	58.4	56.9	35.4	39.8	30.2	34.7

^aHispanic included with Other due to a small number in the sample

^bProportion of Days Covered in the year prior to baseline

^cPills per day

Table 2 - Effects of Breast Cancer Diagnosis on Non-Adherence with Chronic Disease Medications

	% Non-Adherent					
Medication for:	Breast Cancer	Comparison	Absolute Difference	Odds ^{a,b} Ratio	95% CI ^d	p
<i>Non-adherence = PDC^c < 70%</i>						
Diabetes	18.5	14.0	4.5	1.42	1.01 - 1.99	0.04
Lipid Disorders	22.1	21.1	1.0	1.03	0.81 - 1.31	0.83
Hypertension	10.4	11.1	0.7	0.89	0.71 - 1.10	0.30
<i>Non-adherence = PDC < 80%</i>						
Diabetes	26.2	20.2	6.0	1.44	1.07 – 1.95	0.02
Lipid Disorders	28.9	29.9	-1.0	0.91	0.73 – 1.13	0.39
Hypertension	14.2	15.5	-1.3	0.87	0.71 – 1.05	0.15
<i>Non-adherence = PDC < 90%</i>						
Diabetes	34.9	29.4	5.5	1.32	1.00 – 1.74	0.05
Lipid Disorders	44.3	43.7	0.6	0.98	0.81 – 1.20	0.86
Hypertension	20.3	24.1	-3.8	0.76	0.64 – 0.90	<0.01

^aAdjusted for Race, Age, and Pill Burden

^bBreast Cancer vs. Comparison

^cProportion of Days Covered

^dConfidence Interval

Table 3 - Effects of Breast Cancer Diagnosis on Non-Persistence with Chronic Disease Medications

Medication for:	% Non-Persistent		Absolute Difference	Hazard ^{a,b} Ratio	95% CI ^c	p
	Breast Cancer	Comparison				
Diabetes	31.5	26.2	5.3	1.31	1.04 – 1.66	0.02
Lipid Disorders	24.2	24.5	-0.3	0.98	0.80 – 1.19	0.82
Hypertension	18.8	23.8	-5.0	0.73	0.63 – 0.85	<0.01

^aAdjusted for Race, Age, and Pill Burden

^bBreast Cancer vs. Comparison

^cConfidence Interval

Table 4 – Changes in Chronic Disease Medication Non-Adherence from the Pre-Baseline to the Post-Baseline Period Among Breast Cancer Patients and Comparison Women

	Breast Cancer		Comparison			
Medication for:	Odds Ratio ^a	95% CI ^b	Odds Ratio ^a	95% CI ^b	Ratio of Odds Ratios ^c	p-value ^d
<i>Non-adherence = PDC < 70%</i>						
Diabetes	2.10	1.43 – 3.09	1.69	1.37 – 2.07	1.24	0.32
Lipid Disorders	1.51	1.16 – 1.97	1.84	1.61 – 2.11	0.82	0.20
Hypertension	2.34	1.74 – 3.14	2.12	1.85 – 2.43	1.10	0.55
<i>Non-adherence = PDC < 80%</i>						
Diabetes	1.94	1.42 – 2.65	1.44	1.22 – 1.70	1.35	0.09
Lipid Disorders	1.20	0.95 – 1.50	1.64	1.47 – 1.83	0.73	0.02
Hypertension	1.63	1.31 – 2.02	1.73	1.55 – 1.92	0.94	0.64
<i>Non-adherence = PDC < 90%</i>						
Diabetes	1.51	1.17 – 1.96	1.16	1.01 – 1.33	1.31	0.07
Lipid Disorders	1.28	1.05 – 1.55	1.41	1.28 – 1.56	0.90	0.36
Hypertension	1.25	1.06 – 1.48	1.36	1.26 – 1.48	0.92	0.36

^aPost-Baseline Non-Adherence Odds vs. Pre-Baseline Non-Adherence Odds

^bConfidence Interval

^cBreast Cancer Odds Ratio vs. Comparison Odds Ratio

^dTest for Significance of the Relative Difference

^eProportion of Days Covered

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Kaplan-Meier Plot

Figure 1

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Kaplan-Meier Plot

Figure 2

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Kaplan-Meier Plot

Figure 3

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Author/s:

Santorelli, ML;Steinberg, MB;Hirshfield, KM;Rhoads, GG;Bandera, EV;Lin, Y;Demissie, K

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