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POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER PATIENTS WITH BREAST AND COLORECTAL CANCER

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Abstract

Purpose—Our objective was to determine patient characteristics associated with potentially inappropriate medication (PIM) use and its impact on outcomes in patients with breast or colorectal cancer receiving adjuvant chemotherapy.

Patients and Methods—We used the SEER database linked to Medicare claims. Our cohort included patients ≥ 65 years diagnosed with Stage II/III breast or colorectal cancer between 7/1/2007–12/31/2009. The Drugs to Avoid in the Elderly (DAE) and Beers Criteria identified PIM use. Univariate/multivariable logistic regression determined the association of baseline PIMs with covariates. Event-free survival (EFS) was defined from chemotherapy initiation to the first ER visit, hospitalization, death, or a composite until 3 months after chemotherapy. Cox proportional hazards modeling determined association of PIMs with EFS.

Results—The analysis included 1595 breast and 1528 colorectal patients. Baseline PIM frequency was 22.2% (DAE) and 27.6% (Beers) in the breast cohort, and 15.5% (DAE) and 24.8% (Beers) in the colorectal. 37.5% breast patients had at least one adverse outcome; associations included use of ≥ 5 medications, advanced stage, higher comorbidity, and prior ER visits/hospitalizations. Baseline PIM using DAE was associated with increased risk of death in breast patients. 45% colorectal patients had at least one adverse outcome, and associations included taking ≥ 5 medications, older age, female gender, and higher comorbidity. Time-to-event analysis revealed no association between baseline PIM and most outcomes.

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Conclusion—Our findings require further prospective confirmation but support a correlation between polypharmacy and adverse outcomes in cancer patients, questioning the association with PIM.

Keywords

geriatric oncology; health outcomes; breast cancer; colorectal cancer; polypharmacy; inappropriate medication use

INTRODUCTION

Polypharmacy and potentially inappropriate medication (PIM) use is highly prevalent in older patients with cancer, and is recognized as a potential risk factor for adverse outcomes during cancer treatment.¹ Older adult patients with cancer are at high risk for PIM use, as they not only receive medications that treat their medical comorbidities and malignancy, but those to treat therapy-induced toxicity.^{2–4} Furthermore, oncology patients are often seen by many different physicians, and may receive medications for overlapping indications.^{5,6} The National Comprehensive Cancer Network Guidelines for Senior Adult Oncology recommend review of medications for appropriate use at every visit, through screening tools validated in the general older adult population.¹

PIMs are medications or classes of drugs that have been deemed to have a high risk-to-benefit ratio, and should thus be avoided in older persons.⁷ Specific examples of classes deemed to be inappropriate include sedatives (e.g., benzodiazepines) and anticholinergic drugs (e.g., antispasmodics). The most commonly used measure of PIM is the Beers Criteria.⁸ The Healthcare Effectiveness Data and Information Set (HEDIS) Drugs to Avoid in the Elderly (DAE) list include the highest-risk medications from the Beers list.^{9,10} Both have been developed through expert consensus. Amongst older adults in the general population, PIM use is predictive of significant morbidity, more adverse drug events, increased emergency department visits, increased hospitalization, and increased risk of mortality.^{7,11–13} However, there is a dearth of evidence suggesting that these tools are applicable to the older adult cancer population receiving chemotherapy.¹

Several studies have found a high prevalence of PIM use in older cancer patients, ranging from 21% to 40% depending on the criteria used to define PIM. The impact of PIM use on adverse outcomes has not been widely studied, but one study of older adults receiving chemotherapy found no association between PIM use and chemotherapy toxicity or hospitalizations. However, this population was heterogeneous, including patients with different cancer types and a high proportion with advanced disease. The purpose of this study was to evaluate the impact of PIM use on clinical outcomes in a population of breast or colorectal cancer patients receiving adjuvant therapy. Our objective was to identify patient and disease characteristics associated with baseline PIM use defined by the Beers Criteria and DAE and the impact of baseline PIM use on health outcomes during adjuvant chemotherapy.

PATIENTS AND METHODS

Data Source

We used the merged Surveillance, Epidemiology and End Results (SEER)-Medicare database as our data source. The SEER database is a population-based tumor registry sponsored by the National Cancer Institute that contains information on all newly diagnosed cancer cases that occur in persons residing in participating areas.¹⁴ It includes approximately 28% of the US population, and collects information on patient demographics, tumor characteristics, stage, date of diagnosis, treatment, and date and cause of death. Medicare claims data are linked with SEER and include outpatient, inpatient and physician claims. Part D Prescription Drug Events (PDE) files include beneficiary identifiers that have been linked with Medicare claims files, and include drug name, fill date, National Drug Code (NDC) number, quantity dispensed, number of days' supply, cost and other plan-based variables.¹⁴

Study Population

This study included individuals diagnosed between 7/1/07 and 12/31/09 with American Joint Committee on Cancer Modified third edition Stage II and III breast or colorectal cancer, age 66 years or older, who received adjuvant chemotherapy.¹⁵ Identified individuals were required to have Medicare Part A and B coverage starting a minimum of 12 months prior to and after diagnosis, and Part D coverage from 4 months prior to 12 months after diagnosis. Patients who were members of a health maintenance organization at any time during the 1 year before and after diagnosis were excluded given incomplete claims. Men with breast cancer were excluded.

Measures

We used the Common Procedure Terminology J-codes in the SEER-Medicare Outpatient, Physician/Supplier and Durable Medical Equipment files to identify adjuvant chemotherapy use. To be considered adjuvant chemotherapy, claims had to begin within 6 months of diagnosis. The end date of active treatment was determined based on the appearance of final J-codes for chemotherapy, with no further treatment administered for at least a 90-day period. For breast cancer, regimens were classified as an anthracycline-based regimen if J codes for doxorubicin, epirubicin, or mitoxantrone were present. For colorectal cancer, regimens were determined to be multi-agent if they contained oxaliplatin-based J codes. Comorbid conditions present during 1 year prior to diagnosis of cancer were determined using the International Classification of Disease (ICD-9) diagnosis and procedure codes to search the Medicare inpatient, outpatient and physician claims data. Comorbidity score was calculated using Klabunde's adaptation of the Charlson comorbidity index from the macro provided by the National Cancer Institute.¹⁶ Education and poverty are provided as census tract-level variables, and identified the percentage of patients with < 12 years of education or those living below the poverty line

Statistical Analysis

The first objective was to determine the prevalence of baseline PIM use and associated characteristics in older adult patients with breast or colorectal cancer receiving chemotherapy in the adjuvant setting. PIM use was defined based on the 2012 Beers Criteria and DAE list.¹⁰ Both tools have been used for retrospective application to administrative data.⁹ The exposure period for detecting baseline PIMs ranged 4 months before diagnosis up to the date of diagnosis. Medications were included if patients received a single prescription for at least a 90 days' supply or a 30 days' supply prescription with more than 1 refill. Each of these tools resulted in a dichotomous measure of PIM usage (present or absent). PIM rates were also evaluated during the periods 0 to 3 and 3 to 6 months after chemotherapy initiation.

Demographic variables included patient age group, race/ethnicity, sex, census tract-based education and poverty levels. Clinical variables included year of diagnosis, stage, Charlson Comorbidity Index, baseline number of medications, baseline number of outpatient providers and chemotherapy regimen

PIM rates and other baseline sample characteristics were summarized for each cohort using descriptive statistics. Univariate and multivariable logistic regression were used to examine the association of study covariates with each PIM usage measure. Covariates associated with PIM at the 0.2 significance level were candidates for the multivariable model, and those variables with p-values < 0.05 were retained with application of a backward model selection. Statistically and clinically significant variables were retained in the final model, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs).

A second objective of the study was to determine whether baseline PIM use in older adults receiving chemotherapy was predictive of poor clinical outcomes: emergency room (ER) visits, hospitalization, death, and a composite of the three. We evaluated the two measures of PIM (i.e., Beers Criteria and DAE list) separately. Time-to-event and event-free survival (EFS) were measured from the date of first chemotherapy to the date of first outcome or last follow-up if no outcome occurred (designated as 3 months following last chemotherapy). Patients were right-censored at 3 months after the last chemotherapy. Hospitalization was defined as having one or more claims for a hospital stay, and was found in Medicare Provider Analysis and Review (MEDPAR) files. ER visits were similarly defined and derived from Medicare Part B data files. Finally, mortality was considered to be death from any cause. The same independent variables used in the analysis of predictors of baseline PIM were included in the analysis of adverse outcomes.

Cox proportional hazards models were fit to determine the association of patient and clinical characteristics with time-to-outcome endpoints, and the assumption checked for the primary predictor (PIM use). Variables retained in the final model were based on both statistical and clinical significance. Results were expressed in hazard ratios (HRs) and 95% CIs. P-values less than 0.05 were considered to be statistically significant, and all tests were two-sided. All statistical analyses were performed in SAS Version 9.3 (SAS Institute, Cary NC). This study was reviewed and approved by our Institutional Review Board.

RESULTS

The final analysis included 1595 breast and 1528 colorectal cancer patients. Baseline characteristics are shown in Table 1. The frequency of baseline PIM by DAE and Beers Criteria ranged from 15.5% to 27.6%. Other than DAE in the breast cancer cohort, at a time interval of 0-3 months after initiation of chemotherapy, the frequency of PIM use in both cohorts was higher (Table 2). In all cases, PIM use was lower at an interval 3-6 months following initiation of chemotherapy.

Table 3 shows the results of univariate and multivariable analysis of baseline PIM use. For the breast cancer cohort in the multivariate analysis, baseline PIM by both criteria was associated with baseline use of ≥ 5 medications and younger age. Among the colorectal cancer cohort, PIM use was associated with female gender, and baseline use of ≥ 5 medications. There was an association with younger age and baseline PIM by DAE, and non-Hispanic white race using Beers Criteria.

In the time-to-event analysis, the median follow-up for the breast cancer cohort was 5.7 months (0-9 months; Table 4). The one-year EFS rate for the composite outcome was 45% (95% CI, 42%-48%). In multivariable analysis there was an association of increased risk of ER visits with older age, advanced stage, higher comorbidity, baseline use of ≥ 5 medications, and baseline ER visits. An increased risk of hospitalization was associated with Hispanic race, advanced stage, higher comorbidity score, and baseline use of ≥ 5 medications. An increased risk of death was associated with older age, advanced stage, and baseline PIM defined by DAE. Finally, 37.5% patients experienced a composite outcome, and was associated with advanced stage, higher comorbidity, baseline use of ≥ 5 medications, and higher numbers of ER visits or hospitalizations in the year prior. Baseline PIM usage defined by DAE was only associated with overall survival in the time-to-event analysis, and there were no other associations between baseline PIM by either criteria and other outcomes (Table 5).

In the colorectal cancer cohort, the median follow-up was 5.9 months (0-9 months), with a one-year EFS of 38% (95% CI, 35%-41%) for the composite outcome (Table 4). An increased risk of ER visits was associated with older age, female gender, higher comorbidity, non-Hispanic white race, baseline use of ≥ 5 medications, and baseline ER visits. Increased risk of hospitalization was associated with older age, female gender, non-Hispanic white race and higher comorbidity. Death was associated with older age and higher comorbidity. Finally, 45% had a composite outcome, and was associated with older age (age 76-80 vs. 66-70), female gender, race (other v. non-Hispanic white), advanced stage (AJCC stage III v. II), higher comorbidity (score 1 v. 0), baseline number of medications (11+ v. 0-4, and history of ER visits/hospitalization in the prior year. Similar to the breast cancer cohort, there was no association of baseline PIM use and any outcome (Table 6).

DISCUSSION

In this study, we found no association between baseline PIM use and adverse outcomes, including ER visits, hospitalizations, and death, in patients with breast or colorectal cancer

receiving adjuvant chemotherapy. We did find that PIM use was prevalent, ranging from 16% to 25% at baseline, depending on the criteria applied, and associated with various patients characteristics. Our findings are consistent with Maggiore, et al. who noted a rate of PIM usage of up to 29% amongst cancer patients using the Beer's criteria, and did not find an association between PIM use and adverse outcomes. The rate of PIM use was less than that noted by Nightingale et al. where rates ranged from 21-40%.^{17,18}

Similar to prior studies in the general geriatrics population, a higher number of medications was associated with adverse outcomes in both the breast and colorectal cancer cohorts, with implications that polypharmacy is an important risk factor. In both groups, taking 5 medications at baseline was associated with adverse outcome. In the multivariable analysis, there was no association between baseline PIM use and most adverse clinical outcomes. The only association of significance in the time-to-event analysis was PIM defined by DAE and death in the breast cancer cohort. However, given the inconsistency of these findings, no firm conclusions can be made.

We expected to find an association between PIM use and adverse outcomes in older patients receiving chemotherapy. Maggiore's study found no association between PIMs and outcomes, but the study population included 500 patients age 65 and older, a majority (61%) of whom had advanced or metastatic disease. We focused our study on patients receiving adjuvant therapy, presumably with curative intent. We believed that in this group of patients it might be particularly important to optimize medication use and avoid PIMs, and that in a population of patients with advanced disease, certain PIMs might be appropriately used in the provision of supportive care. However, unlike our study, Maggiore found no association between medication number and outcomes. They also evaluated other high-risk drug classes not considered PIMs (anticoagulants, antiplatelets, opioids, insulin, oral hypoglycemics and antiarrhythmics) and found no association with outcome. An advantage of Maggiore's study was that it was prospective, capturing a large amount of patient specific data. The limitation of the Maggiore study was that the evaluation of polypharmacy and PIM use was cross-sectional and performed in a secondary analysis, with limited data on certain components of medications use (such as dosage, frequency, and indication).

As noted, some studies have shown a higher-frequency of PIM usage. Nightingale et al conducted a study of pharmacist-led medication assessment in 248 adults with a mean age of 80, 87% of whom had solid tumors, and 16.3% with advanced stage disease.¹⁷ In addition to capturing information on number of medications (where polypharmacy was defined as 5 medications and excessive polypharmacy as 10 medications), PIM use was categorized using the 2012 Beers Criteria, the Screening Tool of Older Person's Prescriptions (STOPP) criteria, and HEDIS DAE list. The mean number of medications used was 9.23, with the prevalence of polypharmacy and excessive polypharmacy of 41% and 43% respectively. The frequency of PIM use was noted to be 40% utilizing Beers Criteria, 38% with STOPP, and 21% with DAE. The higher incidence of PIM use in this particular study is likely due to the fact that they were able to capture information on over-the counter medications, such as non-steroidal anti-inflammatory drugs (NSAIDs) and first-generation antihistamines.

Finally, in our study, we identified that certain patient and disease characteristics were associated with PIM use. In both cohorts, use of 5 medications at baseline was associated with PIM use in the multivariable analysis. Interestingly, a relatively younger age group of (< 80 years old) was also associated with PIM use. Finally, in the colorectal cancer patients specifically, female gender was also associated with baseline PIM. The association of polypharmacy and PIM use has been corroborated in several publications, including those by Nightingale and Prithviraj.^{17,19} Prithviraj et al found that patients taking 5 medications were significantly more likely to be prescribed a PIM defined by the 2012 Beers Criteria. The authors identified that these patients were also likely to have a poorer functional status or have 5 comorbidities. Nightingale and colleagues similarly found a significant association between number comorbidities and ECOG performance status. A factor unique to our analysis was the association of a relatively younger age group with higher rates of PIM use at baseline.

One major strength of our study was the inclusion of a large number of patients that were homogenous in regard to their disease stage and treatment indication. However, the major limitation in our study was that it was retrospective, with the ability to include only a limited amount of data regarding patient and disease related characteristics as well as medications. Additionally, we only captured a cross-sectional assessment of PIM use. We did try to account for this by only considering medications for which there was a 90-day supply or multiple refills. Furthermore, Medicare Part D data does not include over-the-counter medications such as NSAIDs and antihistamines, which have been captured in previous studies as prevalent medication classes considered PIMs.

The results of our study suggest that although polypharmacy was associated with adverse outcomes, PIMs were not associated with poor clinical outcomes in cancer patients receiving systemic therapy. It is possible that patients did not actually continue to take PIMs once they were diagnosed with cancer and initiated chemotherapy. In addition, several supportive care medications that are considered PIMs may carry more benefit than harm for this select group of patients. Conversely, it may be that there are specific drugs or classes that carry the greatest risk, and should be looked at with greater scrutiny. Furthermore, the more relevant outcome of PIM use in patients with cancer may be quality-of-life issues and financial toxicity, which are of greatest import in the context of advanced stage disease. In order to determine this, more prospective studies are required, that accurately capture polypharmacy, PIM use and adherence to PIM agents in various patient and treatment settings. Baseline data in such studies should also include components of the geriatric assessment, in order to control for confounding factors related to comorbidity and frailty that may account for discrepant outcomes. However, our findings call into question the attention to which clinicians should invest to the screening of PIM use in our older adult cancer patients. Concurrently, they also support an effort to reduce polypharmacy as a way of potentially reducing adverse outcomes.

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TABLE 1

Patient Characteristics

	Breast Cancer Cohort (N = 1595)	Colorectal Cancer Cohort (N = 1528)
Race		
White, non-Hispanic	1212(76.0%)	1127(73.8%)
Black, non-Hispanic	176(11.0%)	113(7.4%)
Hispanic	120(7.5%)	140(9.2%)
Other	87(5.5%)	148(9.7%)
Gender		
Male	0%	758(49.6%)
Year of first diagnosis		
2007	319(20.0%)	318(20.8%)
2008	658(41.3%)	615(40.2%)
2009	618(38.7%)	595(38.9%)
Age at diagnosis		
66 - 70	712(44.6%)	563(36.8%)
71 - 75	497(31.2%)	442(28.9%)
76 - 80	240(15.0%)	348(22.8%)
>80	146(9.2%)	175(11.5%)
Stage		
II	1062(66.6%)	402(26.3%)
III	533(33.4%)	1126(73.7%)
Charlson Comorbidity Index		
	Breast Cancer Cohort	Colorectal Cancer Cohort
0	923(57.9%)	856(56.0%)
1	440(27.6%)	402(26.3%)
2+	232(14.5%)	270(17.7%)
Percent below the poverty level		
Lowest quartile	400(25.1%)	382(25.0%)
Second quartile	399(25.0%)	383(25.1%)
Third quartile	396(24.9%)	381(25.0%)
Highest quartile	398(25.0%)	381(25.0%)
Percent with a high school education (Breast cancer)		
Lowest quartile	399(25.0%)	382(25.0%)
Second quartile (24.08% - 30.84%)	400(25.1%)	383(25.1%)
Third quartile (30.84% - 37.25%)	396(24.9%)	381(25.0%)
Highest quartile (37.25% - 53.53%)	398(25%)	381(25.0%)
Number of care providers at baseline		
0-1	652(40.9%)	669(43.8%)

	Breast Cancer Cohort (N = 1595)	Colorectal Cancer Cohort (N = 1528)
2-3	722(45.3%)	638(41.8%)
4+	221(13.9%)	221(14.5%)
Number of different medications at baseline		
0-4	420(26.3%)	440(28.8%)
5-10	667(41.8%)	627(41.0%)
11+	508(31.8%)	461(30.2%)
Chemo regimen (breast cancer)		
Anthracycline-based	493(30.9%)	
Non-Anthracycline-based	1102(69.1%)	
Chemo multi-regimen (colorectal cancer)		
No		670(43.8%)
Yes		858(56.2%)

TABLE 2

Frequency of PIM use during different time periods

		Breast Cancer Cohort	Colorectal Cancer Cohort
Measure	Period	Frequency	Frequency
DAE	Baseline	354/1595 (22.2%)	237/1528 (15.5%)
	Pre-Chemo	397/1595 (24.9%)	302/1528 (31.3%)
	0-3 mos	351/1595 (22.0%)	306/1528 (20.0%)
	3-6 mos	77/685 (11.2%)	84/759 (11.1%)
Beers	Baseline	440/1595 (27.6%)	379/1528 (24.8%)
	Pre-Chemo	545/1595 (34.2%)	478/1528 (31.3%)
	0-3 mos	531/1595 (33.3%)	442/1528 (28.9%)
	3-6 mos	124/685 (18.1%)	127/759 (16.7%)

TABLE 3

Clinical Characteristics Associated w/Baseline PIM use

PIM Measure	Breast Cancer Cohort		Colorectal Cancer Cohort	
DAE				
Characteristic	Univariate OR (95% CI), p-value	Multivariable OR (95% CI), p-value	Univariate OR (95% CI), p-value	Multivariable OR (95% CI), p-value
Age at Diagnosis				
66-70	Ref		Ref	
71-75	0.89 (0.68-1.17), p=0.4000	0.83 (0.62-1.11), p=0.2100	0.97 (0.69-1.35), p=0.8400	0.86 (0.61-1.22), p=0.3900
76-80	0.88 (0.62-1.24), p=0.4600	0.79 (0.55-1.14), p=0.2100	0.77 (0.53-1.12), p=0.17	0.66 (0.44-0.97), p=0.0350
>80	0.56 (0.35-0.91), p=0.0200	0.44 (0.27-0.72), p=0.0010	0.55 (0.32-0.94), p=0.0029	0.41 (0.24-0.71), p=0.0020
Gender				
Male	NA	NA	Ref	Ref
Female	NA	NA	1.71 (1.29-2.28), p=0.0002	1.66 (1.24-2.24), p=0.0008
Charlson Comorbidity Index				
0	Ref		Ref	
1	1.4 (1.07-1.84), p=0.0140		1.9 (1.37-2.63), p= 0.0001	
2+	1.71 (1.23-2.38), p=0.0010		2.54 (1.79-3.61), p= <0.0001	
# Care Providers				
0-1	Ref		Ref	
2-3	1.35 (1.04-1.76), p=0.0230		1.11 (0.82-1.51), p=0.5000	
4+	1.85 (1.3-2.62) p=0.0006		1.46 (0.98-2.17), p= 0.0600	
# Different Medications				
0-4	Ref		Ref	
5-10	2.99 (1.99-4.5), p= <0.0001	3.14 (2.09-4.73), p<0.0001	3.81 (2.29-6.35), p= <0.0001	4.07 (2.41-6.87), <0.0001
11+	7.24 (4.84-10.84), p=<0.0001	7.67 (5.11-11.5), p=<0.0001	8.33 (5.04-13.78), p= <0.0001	8.84 (5.26-14.84), p<0.0001
Beers				
Characteristic	Univariate OR (95% CI), p-value	Multivariable OR (95% CI), p-value	Univariate OR (95% CI), p-value	Multivariable OR (95% CI), p-value
Race				
Non-Hispanic White	Ref		Ref	Ref
African American	0.95 (0.66-1.35)		0.67 (0.41-1.1)	0.6 (0.36-1), p = 0.049
Hispanic	0.94 (0.62-1.44)		0.7 (0.45-1.09)	0.65 (0.41-1.04), p = 0.0700
Other	0.99 (0.61-1.61)		1.28 (0.88-1.87)	1.13 (0.76-1.69), p = 0.5500
Gender				
Male	NA	NA	Ref	Ref
Female	NA	NA	1.53 (1.21-1.93), p=0.0004	1.35 (1.05-1.73), p=0.0200
Charlson Comorbidity Index				
0	Ref		Ref	
1	1.71 (1.33-2.21), p<0.0001		1.83 (1.39-2.41), p<0.0001	

PIM Measure	Breast Cancer Cohort		Colorectal Cancer Cohort	
2+	2.58 (1.9-3.5), p<0.0001		2.56 (1.89-3.46), p<0.0001	
Number of Care Providers				
0-1	Ref		Ref	
2-3	1.54 (1.2-1.96), p=0.0006		1.13 (0.87-1.46), p=0.3500	
4+	1.89 (1.35-1.53), p=0.0020		1.94 (1.39-2.7), p<0.0001	
Number of Different Medications				
0-4	Ref	Ref	Ref	Ref
5-10	3.44 (2.36-5.01), p<0.0001	3.44 (2.36-5.01), p<0.0001	4.34 (2.85-6.6), p<0.0001	4.3 (2.82-6.55), p<0.0001
11+	8.45 (5.8-12.31), p<0.0001	8.45 (5.8-12.31), p<0.0001	11.15 (7.33-16.96), p<0.0001	10.94 (7.18-16.68), p<0.0001

* OR = odds ratio, CI = Confidence Interval, NA = Not Applicable, Ref = Reference case other variables with non-significant interactions utilizing DAE included year of first diagnosis, race, AJCC stage, poverty level, high-school education. Variables with non-significant interactions utilizing Beer's included year of first diagnosis, AJCC stage, poverty level, high-school education,

TABLE 4

Summary for time (from first chemo)-to-event (ER, hospitalization, death, composite) for Breast and Colorectal Cohort

	ER	Hospitalization	Death	ER visits/Hospitalization/death
Breast cancer				
Number of events (%)	552 (34.6%)	369(23.1%)	34(2.1%)	598 (37.5%)
Median follow up (months)	5.0	5.1	5.7	5.0
Range follow up (months)	(0, 9)	(0, 9)	(0, 9)	(0, 9)
1-year event-free rate	0.49 (0.46,0.52)	0.62(0.59, 0.65)	0.96 (0.94, 0.97)	0.45 (0.42, 0.48)
Colorectal cancer				
Number of events (%)	621(40.6%)	450(29.5%)	76 (5.0%)	687 (45.0%)
Median follow up (months)	4.3	5.1	5.9	4.2
Range follow up (months)	(0, 9)	(0, 9)	(0, 9)	(0, 9)
1-year event-free rate	0.42 (0.39, 0.45)	0.54 (0.51, 0.58)	0.91 (0.88, 0.92)	0.38 (0.35, 0.41)

Table 5

Cox Proportional Hazards Model for time-to-event by Baseline PIM for Breast Cancer Cohort *

PIM Measure	Time to 1 st ER HR (95% CI, p-value)	Time to 1 st Hospitalization HR (95% CI, p-value)	Overall Survival HR (95% CI, p-value)	Time to 1 st ER/Hospitalization/Death HR (95% CI, p-value)
DAE	0.96 (0.78 to 1.18, p=0.6800)	0.96 (0.75-1.23, p=0.7300)	2.31 (1.07-4.96, p=0.033)	0.96 (0.79 to 1.17, p=0.6800)
Beer's	1.02 (0.85 to 1.24, p=0.8310)	1 (0.79 to 1.26, p=1.0000)	1.86 (0.88 to 3.96, p=0.1100)	0.99 (0.82 to 1.19, p=0.9200)

* Multivariable model were additionally adjusted for year of diagnosis, age at diagnosis, race, stage, comorbidity score, poverty, education, number of baseline care providers, chemo regimen, baseline ER / hospitalization if applicable.

Table 6

Cox Proportional Hazards Model for time-to-event by Baseline PIM for Colorectal Cohort *

PIM Measure	Time to 1 st ER visit HR (95% CI, p-value)	Time to 1 st Hospitalization HR (95% CI, p-value)	Overall Survival HR (95% CI, p-value)	Time to 1 st ER visit/ Hospitalization/Death HR (95% CI, p-value)
DAE	0.99 (0.8 to 1.23, p=0.9400)	1.02 (0.79 to 1.32, p=0.8700)	0.8 (0.4 to 1.59, p=0.5300)	0.96 (0.78 to 1.19, p=0.7200)
Beers	0.96 (0.79 to 1.16, p=0.6500)	1.01 (0.81 to 1.27, p=0.900)	0.8 (0.4 to 1.59, p=0.5300)	0.96 (0.78 to 1.19, p=0.7200)

* Multivariable model were additionally adjusted for year of diagnosis, age at diagnosis, race, stage, comorbidity score, poverty, education, number of baseline care providers, chemo regimen, baseline ER / hospitalization if applicable.