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Prevalence and factors associated with potentially inappropriate medication use in older medicare beneficiaries with cancer

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Abstract

Objective: To assess the factors related to potentially inappropriate medication (PIM) use in elderly patients with cancer, as well as to compare the PIM prevalence in older adults with and without cancer.

Methods: Data from the Surveillance, Epidemiology, and End Results-Medicare-linked base (2009–2011) were accessed to conduct a retrospective study comparing patients with cancers of the breast, colon/rectum, and prostate against a matched population of subjects without cancer. PIM use was defined based on the 2015 Beers Criteria and was quantified using prescription claims. Multivariable logistic regression models were used to assess the associations between the patients' characteristics, clinical factors, and PIM use in patients with cancer based on Beers criteria. Propensity score matching was applied to compare use of PIM in patients with versus without cancer.

Results: PIM usage rates in patients with colorectal and breast cancers were significantly higher than non-cancer-bearing adults; the difference in PIM usage rate was not significantly different in the prostate cancer-matched cohort. The prevalence of inappropriate medication use in the three types of cancers evaluated was directly correlated with number of medications prescribed, treatment with chemotherapy, and co-morbid medical problems.

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Author contributions

XF - study design, data analysis, data interpretation, and manuscript writing and review. GMH - data interpretation, manuscript writing, editing, and review. US - study design, data acquisition, data interpretation and manuscript review. JC - study design, data interpretation, data presentation, and manuscript review. FS - study design, data interpretation, and manuscript review.

Declaration of competing interest

None to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sapharm.2019.12.018>.

Conclusion: Patients diagnosed with cancer were more likely to use PIM compared with their non-cancer counterparts. The updated Beers criteria has the potential to serve as an important tool in geriatric oncology practice but it may still need to take into consideration different cancer types and their respective treatments.

Introduction

One critical medication-related issue among older adults is the prescription and use of potentially inappropriate medications (PIM). Despite being linked to negative health outcomes such as adverse drug events (ADEs), falls, cognitive impairment, health-related quality of life concerns, hospitalization, and even mortality,¹ PIM use is highly prevalent among the elderly in the United States (US). The latter assertion is linked to data from the 2009–2010 Medical Expenditure Panel Survey which showed that 41% of those 65 years of age had at least one prescription for a PIM filled.²

PIM use may be even more critical in elderly patients with cancer.³ Approximately 60% of cancer survivors are 65 years of age or older. It has also been reported that older patients with cancer are more vulnerable and have greater risks due to multiple co-morbidities, polypharmacy, geriatric syndromes, cognitive impairment, and malnutrition.^{1,4,5} In addition, management of the cancer patient often requires supportive care medications which further increases the complexity of the treatment regimen and the likelihood of ADEs, drug-drug or drug-disease interactions, and non-adherence.⁶ All of these characteristics expose older patients with cancer to higher risks of PIM use and its associated adverse consequences.

Recent studies in the cancer population found the prevalence of PIM use ranged from 24% to 48.4%, depending on practice settings and criteria used to assess this problem.^{7–10} However, most of these studies analyzed patients in health care facilities, often involving only one practice setting in a certain geographic region which limited the study to one set, or similar sets of prescribing guidelines and habits.

Beers criteria are the most commonly used tool to capture PIM usage rates in the general geriatric population. These criteria are also recommended for the assessment of PIM use in elderly patients with cancer.^{4,11–15} The 2015 American Geriatrics Society (AGS) Beers criteria, for the first time, added drug-drug interactions, though these interactions have not been assessed in a large-scale study of cancer patients.¹⁶ Additionally, differences of PIMs use based on the 2015 Beers criteria (or any other criteria) have not been analyzed in older adults with and without cancer. The aims of this study were to: 1) assess the prevalence and factors associated with PIM use in patients with breast, colorectal, or prostate cancers using the 2015 version of the Beers criteria; and 2) compare the prevalence of PIM use between older adults with and without cancer diagnoses. This study focused on breast, colorectal, and prostate cancers which are among the most frequently diagnosed cancers with comparatively higher five-year survival rates.

Methods

Conceptual framework

An expanded Anderson behavioral model for health service utilization and evidence related to PIM use were utilized to guide the study.^{17–20} Of note, PIM use could be affected by patient-related factors including (1) predisposing factors that refer to the pre-existing propensity of the patients to have PIM use (e.g., demographics); (2) enabling factors that serve as “methods” enabling the utilization (e.g., insurance coverage); and (3) need factors that reflect the level of health status (e.g., the number of chronic conditions, cancer stage). In addition, PIM use may also be influenced by external characteristics or resources derived from local healthcare system characteristics. As such, data analyses require incorporation of these variables.

Study design

Access to the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked database from January 1, 2009 to December 31, 2011 facilitated data collection enabling the conduct of this retrospective observational study. The date of cancer diagnosis was defined as the index date. One year prior to the index date was considered as the baseline period; the succeeding year was labeled as the follow-up period. The database, which links cancer registries from a variety of geographic regions in the US with Medicare claims, contains clinical, demographic, health utilization, and expenditure information of Medicare beneficiaries with and without cancer diagnoses. Medicare Part D claims were used to assess PIM, the primary outcome of interest; the Area Health Resources File was used to evaluate county-level health-related information.²¹ Approval to conduct this study was obtained from the West Virginia University Institutional Review Board.

Study population

Only Medicare fee-for-service beneficiaries > 65 years of age for the 2010 calendar year were included. Eligible patients had new diagnoses of primary, early (stage 0–3) breast, colorectal, or prostate cancers; and no manifestation of disease during the follow-up period. The primary site variable and the International Classification of diseases for oncology, 3rd Edition (ICD-O-3) histology codes were used to identify the type of cancer during 2010 calendar year. Eligibility criteria also included a minimum of one-year follow up after the index date, continuous enrollment in Medicare Parts A and B for 12 months prior to and following the index date, and enrollment in Medicare Part D for 12 months after the index date. Individuals who were enrolled in a health maintenance organization or the Medicare Advantage Program (due to the lack of data) as well as patients in hospice during the baseline and follow-up period were excluded.

Non-cancer control subjects included a 5% random sample of Medicare beneficiaries with any inpatient or outpatient visits from January 1, 2010 to December 31, 2010. Medicare beneficiaries with any diagnoses of cancers during the study period were excluded in the non-cancer group. Propensity score to match cancer cases based on demographic characteristics, including age, gender, race, geographic regions, and number of chronic conditions at baseline was also incorporated in this study.

Measures

PIM use—The primary outcome of interest was PIM use (Yes, No), which was defined as receiving at least one PIM prescription during the follow-up as based on the 2015 Beers criteria. The follow-up period for observing PIM use was 1-year post-index-date for all patients. In order to select the criteria most feasible for assessing this outcome, the claims data were categorized into the following three components: 1) Section I: PIM use focused on specific drugs to avoid; 2) Section II: PIM use associated with drug-disease or drug-syndrome interactions; and 3) Section III: conditional avoidance of clinically relevant non-anti-infective drug-drug interactions. In order to perform calculations, at least one ICD-9 code of the indicated diseases/syndromes during the baseline and follow-up period when potential drug-disease/syndromes interactions was required. To identify Section III potential drug-drug interactions, at least one-day overlap of taking two (three) or more medications that may lead to potentially clinically important drug-drug interactions was also required.²² Due to inconsistencies regarding data availability, criteria requiring specific prescribing indications, dosing, laboratory results, line of therapy, dosage form of certain special formulations, questionable symptoms or conditions, and disease severity were excluded (Appendix 1).

Covariates—Covariates included in the analyses were sex (female, male), age group at the index date (66–69, 70–75, 75–79, 80), race (white, black, others), geographic regions (Northeast, Midwest, South, West), marital status (yes, no), metropolitan status (yes, no), Medicare and Medicaid dual eligibility (yes, no), cancer stage (0–2, 3), surgical resection of tumor (yes, no), radiation to tumor (yes, no), treatment with chemotherapy (yes, no), the number of chronic conditions according to the Department of Health and Human Services framework (i.e., arthritis, asthma, coronary artery disease, cardiac arrhythmias, congestive heart failure, chronic kidney disease, chronic obstructive pulmonary disease [COPD], dementia, depression, diabetes, hepatitis, hyperlipidemia, HIV, hypertension, osteoporosis, substance abuse disorder, schizophrenia, and stroke),²³ and polypharmacy (yes, no), which was defined as concurrent use of five or more medications for a consecutive interval of at least 60 days.²⁴ Disease diagnoses were identified if we observed at least one inpatient or outpatient claim by using ICD-9 code in the baseline and assessment period. We also included county-level unemployment rate (quartiles), percentages of persons aged ≥ 25 years with less than a high school education at the county level (quartiles), county-level median household income (quartiles), and health professional shortage area (HPSA) of primary care at the county level (part county in the HPSA, whole county in the HPSA, or no county in the HPSA).

Statistical analysis

Characteristics of cancer patients using mean $\pm$ standard deviation for continuous variables and frequencies and percentages for categorical variables are presented. Bivariate associations between PIM use and each potential factor were also assessed using *t*-tests for continuous variables and chi-squared tests for categorical variables. The multivariate analysis took into consideration the potential effect of random clustering of county-level factors by utilization of multilevel logistic regression in order to assess any potential factors associated with PIM use. Model selection was based on likelihood ratio tests, the Akaike

information criterion, and the Bayesian information criterion. However, because there was no evidence that the multi-level logistic regression and regular logistic regression models were different, the latter was selected for the study.

Identification and selection of subjects without cancer was described in the Study Population section above. As non-cancer controls do not have “diagnosis” dates, a random service date in the year of 2010 was selected to serve as the index date for them. The study design of controls was identical to the cancer cohort; and PIM use was measured in the follow-up period.

The cancer sample was stratified based on the three types of malignancies and gender - females with breast cancer, males with prostate cancer, females with colorectal cancer, and males with colorectal cancer. Each group was matched with non-cancer controls at 1:1 ratio nearest-neighbor matching based on the propensity score (PS); parameters of the PS included age group, gender (only for the group of all cancer types vs non-cancer), race, and geographic region. Robustness of the match was evaluated using overlap regions of the PS and standardized differences before and after matching occurred. After PS-based match, chi-squared tests were used to analyze whether differences existed in PIM use between each type of cancer and their non-cancer matched counterparts. Multivariate logistic regression models were also applied adjusting for polypharmacy and the number of chronic conditions.

Results

The study included a total of 9693 patients with primary gender-restricted cancers of the breast ($n = 4869$) and prostate ($n = 4824$). The prevalence rates of PIM use in these two cancers were 63.4% and 49.2%, respectively. Among the 1467 females and 1037 males with cancer diagnoses involving the colon or rectum, the prevalence rates were 71.4% and 66.8%, respectively. Polypharmacy was highest in breast cancer (44.1%), and lowest, though still notable, in prostate cancer (32.5%).

Demographic and other major characteristics of Medicare beneficiaries with these cancer diagnoses are detailed in Table 1. Approximately 84% were Caucasian; a vast majority lived in metropolitan areas; and two-thirds of the beneficiaries resided the West and South-west regions of the US. Dual eligibility rates for Medicaid and Medicare benefits among patients with breast, prostate, and colorectal cancers were 13.3%, 9%, and 18.5% (female: 19.6%; male: 17.1%), respectively. Most of the patients (breast cancer and prostate cancer: ~90%; colorectal cancer: ~70%) were diagnosed with stage (2) disease. Surgical resection of primary breast and colorectal cancers was the preferential treatment option in those diagnosed with early stage disease. About half of the patients with prostate cancer received radiation; another third were treated with chemotherapy. The average number of other comorbid medical problems (mean $\pm$ SD) was highest in colorectal cancer (female: 4.1 ± 2.3 ; male: 3.9 ± 2.3) and lowest in prostate cancer (3.4 ± 2.0).

Results from the logistic regression of PIM use in cancer patients are presented in Table 2. A direct correlation was observed between the likelihood of inappropriate medication use and number of drugs prescribed and chronic conditions, as well as treatment with chemotherapy,

across all three types of cancer. On the other hand, PIM use was not associated with all geographic factors or county-level characteristics. However, regional aberrations regarding PIM in patients with breast cancer were found. Compared to women who lived in the West, prescriptions for PIM were less likely among those living in the Midwest (odds ratio [OR], 95%CI = 0.69, 0.53–0.89, $p = 0.004$) and more likely for those residing in the South (OR, 95%CI = 1.27, 1.01–1.60, $p = 0.04$).

Breast cancer and prostate cancer patients with dual eligibility for Medicare and Medicaid had a higher likelihood of PIM use than those with Medicare only (OR, 95%CI = 1.79, 1.43–2.24, $p < 0.001$; OR, 95%CI = 1.39, 1.11–1.74, $p = 0.004$, respectively). Other significant factors positively associated with PIM use in breast cancer patients were later stage (3) (OR, 95%CI = 1.69, 1.24–2.28, $p = 0.001$), surgery naive (OR, 95%CI = 0.72, 0.53–0.99, $p = 0.04$), and younger age (66–69 vs > 79 years) OR, 95%CI = 0.76, 0.63–0.93, $p = 0.01$). In addition, men with prostate cancer who received radiation therapy had 14% lower odds ($p < 0.001$) of having PIM compared to those who did not. Younger patients with prostate cancer were also more likely to use PIMs (70–74 vs 66–69: OR, 95%CI = 0.78, 0.67–0.91, $p = 0.001$).

Gender-related differences for PIM use were also found among those with colorectal cancer. Females who lived in the counties partially in a HPSA had a lower likelihood of having PIM use than those who lived in the counties entirely within a HPSA (OR, 95%CI = 0.65, 0.48–0.89, $p = 0.01$); and radiation therapy in males was found to be associated with a higher risk of PIM use (OR, 95%CI = 3.25, 1.81–5.84, $p < 0.001$).

Of the specific medications (Section I) to avoid in patients with breast and colorectal cancer, proton-pump inhibitors (~20%), first-generation antihistamines (20% for colorectal cancer, 15% for breast cancer), and antipsychotics (~15%) were the three most common PIMs used; high usage rates of proton-pump inhibitors (14%), benzodiazepines, non-benzodiazepine hypnotics (9%), and first-generation antihistamines (7%) were noted in subjects with prostate cancer. Furthermore, variations in drug-disease interactions were apparent. The most frequently observed drug-disease interactions (Section II) in prostate and colorectal cancers included lower urinary tract symptoms, benign prostatic hyperplasia (colorectal cancer: 10%; prostate cancer: 15%), dementia or cognitive impairment (colorectal cancer: 9%; prostate cancer: 3%), and heart failure (~5%). Dementia or cognitive impairment (6%), heart failure (5%), and delirium (2%) were most often observed in patients with breast cancer. Drugs linked to all three cancers that could manifest drug-interactions (Section III) included anticholinergic-anticholinergic interaction (colorectal and breast cancers: ~13%; prostate cancer 7%), and corticosteroids-nonsteroidal anti-inflammatory agents interactions (~6%) (data not presented in table).

Differences in PIM use between matched pairs of patients with and without cancer were also analyzed (Table 3). Even though patients with cancer were more likely to have PIM use compared with their non-cancer counterpart (59% vs 52.7%, $p < 0.001$), this finding was limited to those with breast or colorectal cancers only. The PIM usage rates for matched subjects with and without breast cancer were 63.4% vs. 56.1%, $p < 0.001$; a similar finding occurred in patients, regardless of gender, with and without colorectal cancer – females,

71.4% vs. 57.1%, $p < 0.001$ and males, 66.8% vs. 49.1%, $p < 0.001$. The difference in PIM use among matched pairs with regard to prostate cancer was not significant. Multivariate analyses of these data produced similar results (Table 3).

When each component of the PIM criteria was further analyzed, patients with breast cancer have higher usage rates regarding specific drugs to avoid (Section I) and drug-drug interactions (Section III) ($p < 0.001$), but lower rates relative to drug-disease interactions (Section II) compared to matched subjects without cancer ($p < 0.001$). Except for one, higher rates of these three components (Section I, Section II, and Section III) were also observed in females and males with colorectal cancer compared to their matched counterparts ($p < 0.001$); the exception being drug-disease interactions (Section II) which was limited to females with and without colorectal cancer ($p < 0.001$). The only difference found in patients with prostate cancer and their matched controls was the higher usage rate in relation to drug-disease interactions (Section II) (21.4% vs. 18.6%, $p = 0.001$).

Discussion

Only a few population-based studies have been reported which evaluated PIM use in cancer patients using the cancer registry and Medicare claims-linked database in the US. To our knowledge this paper is among the first to utilize the most updated criteria to identify the prevalence and pattern of PIM use among elderly patients with three different types of cancer compared to matched non-cancer controls.

The prevalence of PIM use in the current report is higher than previously published data among cancer patients.^{7,8,14,15} The finding may be partially explained by utilization of the 2015 AGS Beers criteria which included not only specific drugs to avoid but also drug-disease interactions and drug-drug interactions. In addition, access to the SEER-Medicare-linked dataset enabled more stringent analyses without constraints related to sample size, follow-up times, as well as differences in practice settings and prescribing habits. The latter is consistent with the contrast between this population-based approach and previous studies that were conducted in single or a restricted number of clinical settings. In essence, a composite of these analytical features indicates that the prevalence of PIM use varies extensively by practice settings and geographic regions.⁷

Significant differences in PIM use rates were found across different types of cancer. For example, the prevalence of PIM usage among patients with breast cancer was 7.3% higher than women without cancer. Higher PIM usage rates relative to avoidance of specific drugs (Section I) and drug-drug interactions (Section III) were 9% and 4.5% in those with breast cancer when compared to those without breast cancer, respectively. Significantly higher rates of PIM use were also established in both female and male patients with colorectal cancer compared to matched counterparts. In contrast, differences in prostate cancer matched pairs were not evident except in drug-disease interaction (Section II). A plausible explanation for the latter finding may be related to the smaller percentage of patients with prostate cancer having higher stage disease compared to those with colorectal cancer. While the same assertion does not appear to be valid when applied to the endocrine-sensitive cancers, the absence of differences in PIM usage rates among the prostate cancer-paired subjects could

be related to treatment of the disease. In addition to hormone-deprivation therapy, chemotherapy is used more frequently in the management of breast cancer. The observed distinctions in prevalence of PIM use across cancer types may also be attributable to tumor biology, performance status, disease prognosis, co-morbidities, and individual requirements for additional palliative medications.

The findings in this study are consistent with other investigators who showed that number of chronic conditions and polypharmacy were significantly associated with higher risks of PIM use in cancer patients.^{7,8} Also consistent with two previously published studies in the non-cancer population is the finding that certain demographic factors such as gender (females > males)^{25,26} and age (younger > older) were more likely to use PIM.¹⁵

One new finding relates to the association between type of cancer treatment and PIM use. Treatment with chemotherapy was consistently associated with inappropriate medication use across all three cancer types in our study. That radiation therapy increased the likelihood of PIM use in colorectal cancer, but not in prostate cancer is likely related to the greater morbid sequelae following radiation (which is usually given in combination with chemotherapy) of the rectum. For breast cancer patients, surgery was associated with a lower likelihood of PIM use, though this alone cannot fully account for this finding as most patients will receive some form of systemic adjuvant therapy. On the other hand, PIM use in those not undergoing surgery may be an indicator of suboptimal cancer care. It is also possible that patient preference or other unobserved factors could have affected treatment decisions as well as PIM use.

When determining the significance of research findings, there is an inherent obligation to address potential confounding issues or study limitations. First, the retrospective nature of this study restricted the ability to establish causality; therefore, a cause-effect relationship was not inferred in the interpretation of the results. Second, using claims data limited the ability to assess all facets in the 2015 AGS Beers criteria. Because not all criteria were assessable, it is possible that the current results may have underestimated the true prevalence of PIM use. Additionally, the dataset did not reveal the actual indication for the PIM used or detail the history or severity of the disease for which the drug was prescribed. As such, some of the medications could have been deemed appropriate which artificially increased the PIM usage rate. Third, that Medicare Part D drugs do not include over-the-counter drugs or complementary and alternative medicaments could have resulted in a lower-than- actual PIM usage rate, which in turn may affect the relationships between the PIM use and the factors examined in this study. Fourth, our study results can be generalized to Medicare enrollees with new primary cancer diagnoses only; PIM use in others having secondary cancers may require further investigation. Fifth, the findings of this study are limited to those patients who survived for at least one year after the diagnosis of the cancer. Patients with shorter survival after diagnosis may have different clinical characteristics and medication profiles. Many of them may likely be in the late stages of cancer; the treatment strategies for this subpopulation may also differ and warrant further studies. Furthermore, though we applied the propensity score matching and multivariate logistic regression when comparing PIM use between cancer and non-cancer groups, it is still possible that our findings might be biased by unobserved factors. In addition, this study focused on PIM use in older adults aged 65

and over, however, PIM use among younger patients with cancer deserves further evaluation and continued studies. In the future studies, it is also important to keep evaluating PIM use with the updated Beers criteria supported by more comprehensive evidence and consider assessing PIM burden in other cancer types.

Conclusion

The 2015 AGS Beers criteria can be important to assist decision-making for the assessment of geriatric oncology practice. Analyses of data pertaining to three of the most frequently diagnosed cancers indicated a high prevalence of PIM use regardless of gender or cancer type. The PIM usage rate was directly correlated with co-morbid medical problems, drugs prescribed, and treatment with chemotherapy.

This study demonstrated that the criteria will need to be tailored to type of cancer and their treatment in order to better predict the adverse outcomes associated with medication use. The findings in this report also suggest implications for future quality improvement efforts among Medicare Part D enrollees such as the development of collaborative medication therapy management interventions targeting PIM use, especially in high-risk elderly patients with cancer. Finally, additional research that examines differences in, and underlying reasons for, PIM use is warranted in order to determine the best strategies for susceptible patients diagnosed with a heterogeneous disease like cancer.

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Appendix

Appendix 1.

Selected criteria to identify potentially inappropriate medication (PIM) use in Medicare beneficiaries with cancer — adapted from the 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
PIM. Section I specific drugs – Table 2. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults				
Anticholinergics				
1	First-generation antihistamines	Brompheniramine	Yes	
		Carbinoxamine		
		Chlorpheniramine		
		Clemastine		
		Cyproheptadine		
		Dexbrompheniramine		
		Dexchlorpheniramine		

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
2	Antiparkinsonian agents	Dimenhydrinate	Yes	
		Diphenhydramine		
		Doxylamine		
		Hydroxyzine		
		Meclizine		
		Promethazine		
		Tripolidine		
3	Antispasmodics	Benztropine	Yes	
		Trihexyphenidyl		
4	Anti-thrombotic	Atropine (excludes ophthalmic)	No	Not included because specific formulation was required
		Belladonna alkaloids		
		Clidinium-chlordiazepoxide		
		Dicyclomine		
		Homatropine (exclude ophthalmic)		
		Hyoscyamine		
		Propantheline		
5	Anti-infective	Scopolamine (exclude ophthalmic)	No	Not included because lab data were required
		Dipyridamole		
		Nitrofurantoin		
Cardiovascular				
6	Peripheral alpha-1 blockers	Doxazosin	Yes	Use of these drugs with at least one diagnosis of hypertension with no diagnoses of hyperplasia of prostate during the baseline or follow-up period was considered as PIM use
		Prazosin		
		Terazosin		
8	Central alpha blockers	Clonidine	No	Not included because first-line therapy was required
		Guanabenz		
		Guanfacine		
		Methyldopa		
		Reserine (>0.1 mg/d)		
9		Disopyramide	Yes	
10		Dronedarone	No	Not included because disease severity required
11		Digoxin	No	Not included because first-line therapy was required
12		Nifedipine	Yes	
13		Amiodarone	Yes	Not included because first-line therapy was required
Central nervous systems				
14	Antidepressants	Amoxapine	Yes	
		Clomipramine	Yes	

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
15	Antipsychotics	Desipramine	Yes	Not included because dosage was required
		Doxepin > 6 mg/d	No	
		Imipramine	Yes	
		Nortriptyline	Yes	
		Paroxetine	Yes	
		Protriptyline	Yes	
		Trimipramine	Yes	
15	Antipsychotics		Yes	Any diagnoses of schizophrenia and bipolar disorder during baseline and follow-up period were considered as appropriate use.
16	Barbiturates	Amobarbital	Yes	
		Butabarbital		
		Butalbital		
		Mephobarbital		
		Pentobarbital		
		Phenobarbital		
		Secobarbital		
17	Benzodiazepines	Alprazolam	Yes	
		Estazolam		
		Lorazepam		
		Oxazepam		
		Temazepam		
		Triazolam		
		Clorazepate		
		Chlordiazepoxide (alone or in combination with amitriptyline or clidinium)		
		Clonazepam		
		Diazepam		
18		Flurazepam	Yes	
		Quazepam		
18		Meprobamate	Yes	
19	Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics	Eszopiclone	Yes	
		Zolpidem		
		Zaleplon		
20		Ergoloid mesylates isoxsuprine	Yes	
Endocrine				
21	Androgens	Methyltestosterone	No	Not included because specific condition was required
		Testosterone		
22		Desiccated thyroid	Yes	

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
23		Estrogens with or without progestins	No	Not included because dosage and inexplicit symptoms were required
24	Growth hormone		No	Not included because injectable formulation was required
25	Insuline, sliding scale		No	Not included because injectable formulation was required
26		Megestrol	Yes	
27	Sulfonylureas	Chlorpropamide	Yes	
		Glyburide	Yes	
Gastrointestinal				
28		Metoclopramide	Yes	If with any diagnoses of gastroparesis in the baseline and follow-up periods were considered as appropriate use
29		Mineral oil, given orally	Yes	
30	Proton-pump inhibitors		Yes	Any continuous use of over 60 days during the one-year follow-up period was considered as PIM
Pain medications				
31		Meperidine	Yes	
32	NSAIDs	Aspirin > 325 mg/d (exclude)	No	Not included because dosage was required
		Diclofenac	Yes	Over 180 days during the first-year follow-up period was considered as PIM
		Diflunisal		
		Etodolac		
		Fenoprofen		
		Ibuprofen		
		Ketoprofen		
		Meclofenamate		
		Mefenamic acid		
		Meloxicam		
		Nabumetone		
		Naproxen		
		Oxaprozin		
		Piroxicam		
		Sulindac		
		Tolmetin		
33		Indomethacin	Yes	
		Ketorolac		
34		Pentazocine	Yes	
35	Skeletal muscle relaxants	Carisoprodol	Yes	
		Chlorzoxazone		
		Cyclobenzaprine		
		Metaxalone		

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
36	Genitourinary	Methocarbamol		
		Orphenadrine		
		Desmopressin	Yes	Patients with any diagnoses of nocturia or nocturnal polyuria in the baseline and follow-up periods were considered as PIM users
PIM. Section II potential disease-drug interactions - Table 3. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interaction That May Exacerbate the Disease or Syndrome				
	Disease or syndrome	Drugs		
37	Heart failure	• NSAIDs and cox-2 inhibitors	Yes	
		• Nondihydropyridine ccbs-avoid only for heart failure with reduced ejection fraction	No	Not included because specific indication was required
			Yes	
		• Thiazolidinediones (pioglitazone, rosiglitazone, cilostazol)	No	Not included because disease severity was required
		• Dronedarone (severe or recently de-compensated heart failure)		
38	Syncope	• AChEIs	Yes	
		• Peripheral alpha-1 blockers		
		Doxazosin		
		Prazosin		
		Terazosin		
		• Tertiary TCAs		
		• Chlorpromazine		
		• Thioridazine		
		• Olanzapine		
39	Chronic seizures or epilepsy	• Bupropion	Yes	
		Chlorpromazine		
		Clozapine		
		Maprotiline		
		Olanzapine		
		Thioridazine		
		Thiothixene		
		Tramadol		

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
40	Delirium	<ul style="list-style-type: none"> Anticholinergics Antipsychotics Benzodiazepine Corticosteroids H₂-receptor antagonists <ul style="list-style-type: none"> Cimetidine Famotidine Nizatidine Ranitidine Meperidine Sedative hypnotics 	Yes	
41	Dementia or cognitive impairment	<ul style="list-style-type: none"> Anticholinergics Benzodiazepine H₂-receptor antagonists Nonbenzodiazepine, Benzodiazepine receptor agonist Hypnotics <ul style="list-style-type: none"> Eszopiclone Zolpidem Zaleplon Antipsychotics 	No	
42	History of falls or fractures*	<ul style="list-style-type: none"> Anticonvulsants Antipsychotics Benzodiazepine Nonbenzodiazepine, Benzodiazepine receptor agonist Hypnotics <ul style="list-style-type: none"> Eszopiclone Zolpidem Zaleplon TCA SSRIs Opioids 	Yes	

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
43	Insomnia	<ul style="list-style-type: none"> Oral decongestants <ul style="list-style-type: none"> Pseudoephedrine Phenylephrine Stimulants <ul style="list-style-type: none"> Amphetamine Armodafinil Methylphenidate Modafinil Theobromines <ul style="list-style-type: none"> Theophylline Caffeine 	Yes	
44	Parkinson disease	<ul style="list-style-type: none"> All antipsychotics (except aripiprazole, quetiapine, clozapine) Antiemetics <ul style="list-style-type: none"> Metoclopramide Prochlorperazine Promethazine 	Yes	
45	History of gastric or duodenal ulcers*	<ul style="list-style-type: none"> Aspirin (> 325 mg/d) (exclude) Non-COX-2 selective NSAIDs 	No Yes	Not included because dosage was required. If patients took any gastroprotective agent (i.e., PPI or misoprostol) in the follow-up period, these patients were NOT considered as PIM users.
46	Chronic kidney disease stages IV or less (creatinine clearance <30 mL/min)	<ul style="list-style-type: none"> NSAIDs 	No	Not included because lab data and disease severity were required
47	Urinary incontinence (all types) in women	<ul style="list-style-type: none"> Estrogen oral and transdermal (excludes intravaginal estrogen) Peripheral alpha-1 blockers Doxazosin Prazosin Terazosin 	No	Not included because special formulation was required
48	Lower urinary tract symptoms, benign prostatic hyperplasia for male	Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence	Yes	

#	Criteria	Drugs	Inclusion	Reason for exclusion/Notes
PIM. Section III potential drug-drug interactions - Table 5. 2015 American Geriatrics Society Beers Criteria for Potentially Clinically Important Non-Anti-infective Drug-Drug Interactions That Should Be Avoided in Older Adults				
	Drug**	Drug		
49	ACEIs	Amiloride or triamterene	Yes	
50	Anticholinergic	Anticholinergic	Yes	If two or more different anticholinergics were used together for at least one day in the follow-up period based on prescription claims, it was considered as potential drug-drug interaction
51	3 CNS-active drugs		Yes	If three or more different CNS-active drugs were used together for at least one day in the follow-up period based on prescription claims, it was considered as potential drug-drug interaction
52	Corticosteroids	NSAIDs	Yes	
53	Lithium	ACEIs	Yes	
54	Lithium	Loop diuretics	Yes	
55	Peripheral alpha-1 blockers	Loop diuretics	Yes	
56	Theophylline	Cimetidine	Yes	
57	Warfarin	Amiodarone	Yes	
58	Warfarin	NSAIDs	Yes	

Adapted from: American Geriatrics Society 2015 Beers Criteria Update Expert Panel, Fick, D. M., Semla, T. P., Beizer, J., Brandt, N., Dombrowski, R., & Giovannetti, E. (2015). *American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society, 63(11), 2227–2246.*

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Table 1

Descriptive analyses of Medicare fee-for-service beneficiaries with breast, prostate, and colorectal cancer.

		Breast cancer (N = 4869)		Prostate cancer (N = 4824)		Colorectal cancer -female (N = 1467)		Colorectal cancer-male (N = 1037)	
		N	%	N	%	N	%	N	%
Predisposing factors									
Age									
66-69		1238	25.4	1573	32.6	214	14.6	238	22.9
70-74		1302	26.8	1676	34.7	304	20.7	273	26.3
75-79		994	20.4	965	20.0	326	22.2	224	21.6
80+		1335	27.4	610	12.7	623	42.5	302	29.1
Race									
White		4068	83.5	3871	80.2	1159	79.0	812	78.3
Black		395	8.1	476	9.9	147	10.0	72	6.9
Other		406	8.3	477	9.9	161	11.0	153	14.8
Geographic Regions									
Northeast		975	20.0	855	17.7	328	22.4	209	20.2
Midwest		654	13.4	623	12.9	206	14.0	136	13.1
South		1177	24.2	1195	24.8	372	25.4	257	24.8
West		2063	42.4	2151	44.6	561	38.2	435	42.0
Marital status									
No		2867	58.9	1772	36.7	1005	68.5	364	35.1
Yes		2002	41.1	3052	63.3	462	31.5	673	64.9
Metropolitan status									
Yes		3956	81.3	3837	79.6	1150	78.4	818	79.0
No		911	18.7	986	20.4	317	21.6	218	21.0
Enabling factor									
Yes		647	13.3	435	9.0	287	19.6	177	17.1
No		4222	86.7	4389	91.0	1180	80.4	860	82.9
Need factors									
Cancer stage									
stage 0-I-II		4483	92.1	4498	93.2	1077	73.4	737	71.1

stage III	386	7.9	326	6.8	390	26.6	300	28.9
Had surgery								
Yes	4597	94.4	1249	25.9	1258	85.8	852	82.2
No	272	5.6	3575	74.1	209	14.3	185	17.8
Had radiation therapy								
Yes	2756	56.6	2418	50.1	123	8.4	144	13.9
No	2113	43.4	2406	49.9	1344	91.6	893	86.1
Had chemotherapy								
Yes	998	20.5	1576	32.7	334	22.8	271	26.1
No	3871	79.5	3248	67.3	1133	77.2	766	73.9
Polypharmacy								
Yes	2145	44.1	1568	32.5	608	41.5	408	39.3
No	2724	55.9	3256	67.5	859	58.5	629	60.7
Number of chronic conditions at baseline								
	3.7	2.1	3.4	2.0	4.1	2.3	3.9	2.3
Environment factors								
	N	%	N	%	N	%	N	%
County-level unemployment rate								
Q1 [lowest]	1200	24.6	1188	24.6	347	23.7	254	24.5
Q2	1235	25.4	1217	25.2	370	25.2	234	22.6
Q3	1162	23.9	1206	25.0	377	25.7	286	27.6
Q4 [highest]	1272	26.1	1213	25.1	373	25.4	263	25.4
Percentages of persons aged 25 years with less than a high school diploma (county level)								
Q1 [lowest]	1229	25.24	1209	25.1	390	26.6	272	26.2
Q2	1261	25.9	1198	24.8	362	24.7	229	22.1
Q3	1167	23.97	1214	25.2	364	24.8	260	25.1
Q4 [highest]	1212	24.89	1203	24.9	351	23.9	276	26.6
County-level median household income								
Q1 [lowest]	1229	25.2	1208	25.0	380	25.9	253	24.4
Q2	1261	25.9	1328	27.5	404	27.5	307	29.6
Q3	1167	24.0	1090	22.6	333	22.7	222	21.4

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Q4 [highest]	1212	24.9	1198	24.8	350	24.9	255	24.6
County-level HPSA of primary care								
No county in HPSA	600	12.3	537	11.1	152	10.3	114	11.0
Whole county in HPSA	2189	45.0	2288	47.4	686	46.8	514	49.6
Part county in HPSA	2078	42.7	1998	41.4	629	42.9	408	39.4

Notes: Cancer was excluded when we calculated the number of chronic conditions in this study. Abbreviation: SD=Standard Deviation, HPSA = health professional shortage area.

Table 2

Factors associated with potentially inappropriate medication (PIM) use among Medicare beneficiaries with breast, prostate, and colorectal cancer: results from multivariate logistic regression models.

	Colorectal cancer -female (N = 1467)			Colorectal cancer- male (N = 1037)			Prostate cancer (N = 4824)			Breast cancer (N = 4869)		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Predisposing factors												
Age												
70–74 vs 66–69	1.06	(0.67, 1.66)	0.81	1.44	(0.94, 2.20)	0.09	0.78	(0.67, 0.91)	0.001	0.95	(0.79, 1.14)	0.55
75–79 vs 66–69	0.79	(0.51, 1.23)	0.30	1.20	(0.78, 1.87)	0.40	0.86	(0.72, 1.03)	0.10	0.88	(0.72, 1.07)	0.20
80+ vs 66–69	1.10	(1.04, 1.18)	0.70	1.35	(0.89, 2.04)	0.15	0.91	(0.74, 1.13)	0.40	0.76	(0.63, 0.93)	0.01
Race												
AA vs White	0.92	(0.58, 1.46)	0.73	0.88	(0.48, 1.62)	0.69	1.00	(0.80, 1.24)	0.99	0.80	(0.62, 1.03)	0.08
Other vs White	0.95	(0.61, 1.49)	0.84	1.44	(0.89, 2.31)	0.13	1.20	(0.97, 1.49)	0.10	0.78	(0.61, 1.01)	0.05
Geographic regions												
Midwest vs West	0.63	(0.38, 1.04)	0.07	1.00	(0.55, 1.82)	1.00	0.92	(0.73, 1.16)	0.48	0.69	(0.53, 0.89)	0.004
Northeast vs West	0.86	(0.58, 1.28)	0.46	0.91	(0.57, 1.47)	0.71	0.77	(0.63, 0.94)	0.01	0.87	(0.71, 1.06)	0.17
South vs West	1.30	(0.81, 2.10)	0.28	0.86	(0.49, 1.51)	0.60	0.99	(0.80, 1.23)	0.92	1.27	(1.01, 1.60)	0.04
Metropolitan status												
Yes vs No	1.15	(0.77, 1.71)	0.50	0.90	(0.56, 1.45)	0.67	0.86	(0.71, 1.05)	0.14	1.03	(0.84, 1.26)	0.79
Marital status												
Yes vs no	0.78	(0.59, 1.04)	0.09	0.84	(0.61, 1.15)	0.27	1.01	(0.89, 1.15)	0.87	1.10	(0.96, 1.27)	0.17
Enabling factor												
Medicare and Medicaid dual eligibility												
Yes vs No	1.27	(0.88, 1.84)	0.20	1.10	(0.71, 1.70)	0.67	1.39	(1.11, 1.74)	0.004	1.79	(1.43, 2.24)	<0.001
Need factors												
Cancer stage												
Stage III vs 0-I-II	1.15	(0.81, 1.63)	0.45	1.18	(0.79, 1.78)	0.42	0.95	(0.74, 1.21)	0.67	1.69	(1.24, 2.28)	0.001
Had surgery												
Yes vs No	1.24	(0.86, 1.79)	0.25	1.28	(0.86, 1.90)	0.22	-	-	-	0.72	(0.53, 0.99)	0.04
Had radiation therapy												
Yes vs No	1.59	(0.85, 2.98)	0.15	3.25	(1.81, 5.84)	<0.001	0.86	(0.75, 0.98)	0.02	0.95	(0.82, 1.08)	0.41

	Colorectal cancer -female (N = 1467)			Colorectal cancer- male (N = 1037)			Prostate cancer (N = 4824)			Breast cancer (N = 4869)		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Had chemotherapy												
Yes vs No	6.83	(4.24, 11.01)	< 0.001	4.66	(2.85, 7.62)	< 0.001	1.20	(1.04, 1.38)	0.01	4.58	(3.72, 5.61)	< 0.001
Polypharmacy												
Yes vs No	4.12	(3.03, 5.61)	< 0.001	3.23	(2.29, 4.55)	< 0.001	3.25	(2.82, 3.75)	< 0.001	3.39	(2.93, 3.93)	< 0.001
Number of chronic conditions at baseline	1.10	(1.04, 1.18)	0.002	1.16	(1.07, 1.24)	< 0.001	1.16	(1.12, 1.20)	< 0.001	1.09	(1.05, 1.13)	< 0.001
Environment factor												
County-level HPSA for primary care												
No county vs Whole county	0.67	(0.41, 1.11)	0.11	0.85	(0.48, 1.50)	0.57	0.97	(0.76, 1.23)	0.07	1.01	(0.78, 1.29)	0.99
Part county vs Whole county	0.65	(0.48, 0.89)	0.01	0.70	(0.49, 1.01)	0.053	1.03	(0.89, 1.20)	0.67	1.09	(0.92, 1.28)	0.32

Note: The PIM was determined by using the 2015 American Geriatrics Society (AGS) Beers criteria. Section I indicates the specific drugs to avoid. Section II refers to drug-disease interaction. Section III refers to drug-drug interaction. Cancer was excluded when we calculated the number of chronic conditions in this study. Abbreviations: HPSA = health professional shortage area, OR=Odds Ratio, 95% CI = 95% confidence interval.

Table 3

Differences in potentially inappropriate medication use between Medicare beneficiaries with and without cancer after propensity score matching.

	Breast cancer-female			Prostate cancer-male			Colorectal cancer-female			Colorectal cancer-male			All types of cancer		
	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value
	Cancer (N = 4869)	Non-cancer (N = 4869)		Cancer (N = 4824)	Non-cancer (N = 4824)		Cancer (N = 1467)	Non-cancer (N = 1467)		Cancer (N = 1037)	Non-cancer (N = 1037)		Cancer (N = 12,197)	Non-cancer (N = 12,197)	
Variables used for propensity score matching- After matching															
Sex															
Female													6336 (51.9%)	6336 (51.9%)	1.00
Male	-	-											5861 (48.1%)	5861 (48.1%)	1.00
Region			1.00			1.00			1.00			1.00			1.00
NE	975 (20.0%)	975 (20.0%)		855 (17.7%)	855 (17.7%)		328 (22.4%)	328 (22.4%)		209 (20.2%)	209 (20.2%)		2367 (19.4%)	2367 (19.4%)	
MW	654 (13.4%)	654 (13.4%)		623 (12.9%)	623 (12.9%)		206 (14.0%)	206 (14.0%)		136 (13.1%)	136 (13.1%)		1619 (13.3%)	1619 (13.3%)	
South	1177 (24.2%)	1177 (24.2%)		1195 (24.8%)	1195 (24.8%)		372 (25.4%)	372 (25.4%)		257 (24.8%)	257 (24.8%)		3001 (24.6%)	3001 (24.6%)	
West	2063 (42.4%)	2063 (42.4%)		2151 (44.6%)	2151 (44.6%)		561 (38.2%)	561 (38.2%)		435 (41.9%)	435 (41.9%)		5210 (42.7%)	5210 (42.7%)	
Race			1.00			1.00			1.00			1.00			1.00
White	4068 (83.6%)	4068 (83.6%)		3871 (80.2%)	3871 (80.2%)		1159 (79.0%)	1159 (79.0%)		812 (78.3%)	812 (78.3%)		9910 (81.3%)	9910 (81.3%)	
Black	395 (8.1%)	395 (8.1%)		476 (9.9%)	476 (9.9%)		147 (10.0%)	147 (10.0%)		72 (6.9%)	72 (6.9%)		1090 (8.9%)	1090 (8.9%)	
Other	406 (8.3%)	406 (8.3%)		477 (9.9%)	477 (9.9%)		161 (11.0%)	161 (11.0%)		153 (14.8%)	153 (14.8%)		1197 (9.8%)	1197 (9.8%)	
Age			1.00			1.00			1.00			1.00			1.00
66-69	1238 (25.4%)	1238 (25.4%)		1573 (32.6%)	1573 (32.6%)		214 (14.6%)	214 (14.6%)		238 (23.0%)	238 (23.0%)		3263 (26.8%)	3263 (26.8%)	
70-74	1302 (26.8%)	1302 (26.8%)		1676 (34.7%)	1676 (34.7%)		304 (20.7%)	304 (20.7%)		273 (26.3%)	273 (26.3%)		3555 (29.1%)	3555 (29.1%)	
75-79	994 (20.4%)	994 (20.4%)		965 (20.0%)	965 (20.0%)		326 (22.2%)	326 (22.2%)		224 (21.6%)	224 (21.6%)		2509 (20.6%)	2509 (20.6%)	

Breast cancer-female			Prostate cancer-male			Colorectal cancer-female			Colorectal cancer-male			All types of cancer		
N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value
Cancer (N = 4869)	Non-cancer (N = 4869)		Cancer (N = 4824)	Non-cancer (N = 4824)		Cancer (N = 1467)	Non-cancer (N = 1467)		Cancer (N = 1037)	Non-cancer (N = 1037)		Cancer (N = 12,197)	Non-cancer (N = 12,197)	
80	1335 (27.4%)		610 (12.7%)	610 (12.7%)		623 (42.5%)	623 (42.5%)		302 (29.1%)	302 (29.1%)		2870 (23.5%)	2870 (23.5%)	
PIM use after matching														
PIM		<.0001			0.53			<.0001			<.0001			<.0001
Yes	3085 (63.4%)		2371 (49.2%)	2340 (48.5%)		1048 (71.4%)	837 (57.1%)		693 (66.8%)	509 (49.1%)		7197 (59.0%)	6431 (52.7%)	
No	1784 (36.6%)		2453 (50.8%)	2484 (51.5%)		419 (28.6%)	630 (42.9%)		344 (33.2%)	528 (50.9%)		5000 (41.0%)	5766 (47.3%)	
PIM-Section I		<.0001			0.13			<.0001			<.0001			<.0001
Yes	2876 (59.1%)		2075 (43.0%)	2001 (41.5%)		979 (66.7%)	722 (49.2%)		635 (61.2%)	426 (41.1%)		6565 (53.8%)	5600 (45.9%)	
No	1993 (40.9%)		2749 (57.0%)	2823 (58.5%)		488 (33.3%)	745 (50.8%)		402 (38.8%)	611 (58.9%)		5632 (46.2%)	6597 (54.1%)	
PIM-Section II		<.0001			0.001			0.23			<.0001			0.11
Yes	628 (12.9%)		1032 (21.4%)	897 (18.6%)		314 (21.4%)	288 (19.6%)		366 (35.3%)	225 (21.7%)		2340 (19.2%)	2243 (18.4%)	
No	4241 (87.1%)		3792 (78.6%)	3927 (81.4%)		1153 (78.6%)	1179 (80.4%)		671 (64.7%)	812 (78.3%)		9857 (80.8%)	9954 (81.6%)	
PIM-Section III		<.0001			0.13			<.0001			0.001			<.0001
Yes	1232 (25.3%)		740 (15.3%)	795 (16.5%)		399 (27.2%)	305 (20.8%)		223 (21.5%)	165 (15.9%)		2594 (21.3%)	2215 (18.2%)	
No	3637 (74.7%)		4084 (84.7%)	4029 (83.5%)		1068 (72.8%)	1162 (79.2%)		814 (78.5%)	872 (84.1%)		9603 (78.7%)	9982 (81.8%)	
Multivariate logistic regression														
PIM	A OR	P value	AOR		P value	AOR		P value	AOR		P value	AOR		P value

Breast cancer-female		Prostate cancer-male			Colorectal cancer-female			Colorectal cancer-male			All types of cancer		
N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	N (%)	P value	N (%)	P value
Cancer (N = 4869)	Non-cancer (N = 4869)		Cancer (N = 4824)	Non-cancer (N = 4824)		Cancer (N = 1467)	Non-cancer (N = 1467)		Cancer (N = 1037)	Non-cancer (N = 1037)		Cancer (N = 12,197)	Non-cancer (N = 12,197)
1.30 (1.19, 1.42)	1.30 (1.19, 1.42)	<.0001	1.06 (0.97, 1.16)	1.06 (0.97, 1.16)	0.18	1.94 (1.64, 2.28)	1.94 (1.64, 2.28)	<.0001	2.10 (1.74, 2.54)	2.10 (1.74, 2.54)	<.0001	1.30 (1.23, 1.38)	1.30 (1.23, 1.38)
yes vs no													

Note: polypharmacy and number of chronic conditions were adjusted in the multivariate logistic regression models. Cancer was excluded when we calculated the number of chronic conditions in this study. The PIM use was determined by using the 2015 American Geriatrics Society (AGS) Beers criteria. Section I indicates the specific drugs to avoid. Section II refers to drug-disease interaction. Section III refers to drug-drug interaction.

Abbreviation: AOR: adjusted odds ratio; NE: north east; MW: middle west; PIM: potentially inappropriate medication.