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Patient Characteristics Associated with Polypharmacy and Inappropriate Prescribing of Medications among Older Adults with Cancer

Gopi K. Prithviraj, M.D[1], **Siran Koroukian, Ph.D.**[2,3], **Seunghee Margevicius, M.A.**[3], **Nathan A. Berger, M.D.**[1,2,4], **Rakesh Bagai, M.D.**[5], and **Cynthia Owusu, M.D.**[1,2,4]

[1]Department of Medicine, University Hospitals Case Medical Center, Cleveland, Ohio

[2]Case Comprehensive Cancer Center, Cleveland, Ohio

[3]Department of Epidemiology and Biostatistics, Case Western Reserve School of Medicine, Cleveland, Ohio

[4]Division of Hematology/Oncology, University Hospitals Case Medical Center, Cleveland, Ohio

[5]Cleveland Clinic, Cleveland, Ohio

Abstract

OBJECTIVES—To identify patient characteristics associated with polypharmacy and inappropriate medication (PIM) use among older patients with newly diagnosed cancer.

DESIGN—Cross-Sectional Study.

SETTING—Ambulatory oncology clinics at an academic medical center.

PARTICIPANTS—117 patients aged ≥ 65 years with newly diagnosed histologically confirmed stage I–IV cancer were enrolled between April 2008 and September 2009.

Corresponding Author: Cynthia Owusu, MD, MS, Case Western Reserve University School of Medicine, UHHS Seidman Cancer Center-BHC 5055, 11100 Euclid Avenue, Cleveland, OH 44106-5055, Telephone: 216-844-7670, Fax: 216-844-5234, Cynthia.owusu@case.edu.

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Author Contributions:
Conception design: Cynthia Owusu.
Acquisition of data: Cynthia Owusu, Gopi Prithviraj, Rakesh Bagai.
Analysis and interpretation of data: Cynthia Owusu, Gopi Prithviraj, Siran Koroukian, Seunghee Margevicius, Rakesh Bagai, Nathan Berger.
Manuscript writing and approval: Cynthia Owusu, Gopi Prithviraj, Siran Koroukian, Seunghee Margevicius, Rakesh Bagai, Nathan Berger.

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MEASUREMENTS—Medication review, included patient self-report and medical records. Polypharmacy was defined as the concurrent use of ≥ five medications, (*Yes*/*No*). PIM use was defined as use of ≥ one medication included in the 2003 update of Beers Criteria, (*Yes*/*No*).

RESULTS—The prevalence of polypharmacy and PIM use were 80% and 41%, respectively. Three independent correlates of medication use were identified. An increase in comorbidity count by one, ECOG-PS score by one, and PIM use by one, was associated with an increase in medication use by 0.48 (*P*=0.0002), 0.79 (*P*=0.01) and 1.22 (*P*=0.006), respectively. Two independent correlates of PIM use were identified. The odds of using PIMs decreased by 10% for one unit increase in Body Mass Index [Odds Ratio (OR) 0.90, 95% CI = (0.84, 0.97)], and increased by 18% for each increase in medication count by one [OR 1.18, 95% CI = (1.04, 1.34)].

CONCLUSION—There was a high prevalence of polypharmacy and PIM use in older patients with newly diagnosed cancer. Given the co-occurrence of polypharmacy with poor performance status and multi-morbidity, multi-dimensional interventions are needed in the geriatric-oncology population to improve health and cancer outcomes.

Background

In the aging population, polypharmacy and potentially inappropriate prescribing of medication (PIM) is highly prevalent.[1–8] Polypharmacy has been associated with an increased risk of PIM[1, 5, 6, 9, 10] and increased risk of adverse drug events (ADEs), and may increase the risk of falls and geriatric syndromes as well as morbidity and mortality in the elderly population.[6, 11–13]

Oncology patients are often on complex medication regimens, and receive medications not only to treat their malignancy and comorbidities, but also to treat therapy-induced toxicity and conditions related to their malignancy such as deep vein thrombosis and seizures.[5, 14–16]. Oncology patients are also seen by multiple physicians, including an oncologist and a primary care physician, who could prescribe multiple different medications for the same symptoms [5, 17]. Compounding the issue of polypharmacy in oncology patients is the use of herbal medications, as prior data has shown that at least one-third of cancer patients use at least one alternative medication [16, 18]. As such, polypharmacy may be more prevalent in older cancer patients. These medications can interact with the patient's regular medication regimen as well as traditional cancer therapies, causing ADEs[16–18]. Finally, the risk of drug interactions increases with the addition of each antineoplastic agent, placing the patient at risk for further ADEs.[17, 19]

The Beers Criteria were developed from expert consensus to identify potentially inappropriate medications in the elderly population that should be avoided.[2–4, 20]These criteria include drugs with a long half-life, medications with side effects such as sedation or anticholinergic effects, medications that are high risk when safer alternatives exist or are ineffective, doses of drugs that should not be exceeded, and drug-disease and drug-drug interactions that should be avoided in the elderly populations[1–4]. The prevalence of PIM use ranges from 33%–37% of acutely ill patients presenting to hospitals, 28% of elderly community-dwelling residents, 49% of elderly patients presenting to the outpatient primary care clinic and in up to 40% of nursing home residents[1, 2, 8, 21–24]. Use of Beers Criteria Medications among older patients is associated with increased rate of outpatient visits, reduced time to hospitalization, increased frequency of emergency department visits, increased healthcare costs, and increased mortality [5, 7, 9, 21]. Use of PIM's has been shown to be associated with polypharmacy and with ADE's [25, 26]

However, few original studies have examined the presence of polypharmacy and inappropriate prescribing of medications in older cancer patients.[14, 15, 27]The objective of

this study, therefore, was to examine the prevalence of polypharmacy and the inappropriate prescribing of medications, and to determine factors independently associated with polypharmacy and PIM use among older patients with newly diagnosed cancer.

METHODS

PATIENTS and METHODS

Study Design and Patient Population—This is a baseline cross-sectional study nested within a longitudinal study of older cancer patients ≥ 65 years of age with histologically confirmed new cancer diagnosis, irrespective of stage at diagnosis. Participants were recruited from ambulatory oncology clinics at an academic center between February 1, 2008 and September 30, 2009. Participants who had received any prior chemotherapy or radiation therapy for current cancer, were unable to give informed consent or were Non-English speaking (the study relied heavily on instruments mostly validated in English) were excluded. A convenience sample of 121 participants was enrolled of which 117 completed baseline study assessments. Two participants died before baseline assessment could be completed, one withdrew from the study, and another was lost to follow-up. There were no significant differences in baseline characteristics between patients who completed baseline assessment and those who did not. The proportion of newly diagnosed cancer patients age 65–74, and ≥ 75 years in our study cohort (55% and 45%, respectively) and in our institution at large (58% and 42%, respectively) were approximately the same and suggestive that our cohort was representative of our institution's population of older patients with newly diagnosed cancer. The study was approved by the Institutional Review Board at our institution and informed consent was obtained from all participants.

Study Procedures, Measures and Data Collection—New cancer patients were identified from the schedules of medical and radiation oncologists. A research assistant, who was unaware of study outcomes of interest, approached eligible patients for informed consent during patients' initial visit with a medical or radiation oncologist. At study entry, participants completed a Comprehensive Geriatric Assessment (CGA), a multidisciplinary and multidimensional evaluation of the functional, cognitive, psychosocial, comorbidity, and nutritional status of older adults. Medication review entailed recording details of all medications participants were taking (prescribed and non-prescribed by relying on participant self-report and medical records (paper and electronic)). All assessments were completed prior to receipt of any systemic treatment (neoadjuvant, adjuvant or palliative, whichever came first) or radiation therapy. Medical record abstraction was also conducted by a research assistant to collect data on tumor characteristics and cancer treatments received.

Analytic Variables

Primary outcome variables: The primary outcome variables were: 1) polypharmacy defined as the concurrent use of five or more medications[28–30], *Yes or No*; 2) potentially inappropriate prescribed medications (PIMs) based on the 2003 update of the Beers Criteria[2], *Yes or No*. For our definition of PIMs, we included the medication classes in the 2003 update that should generally be avoided in persons aged 65 or older, irrespective of diagnosis.[2] We did not use the criterion based on diagnosis as information on diagnosis may be incomplete.

Explanatory Variables

Socio-demographic characteristics: Variables included sex, age (65–74, ≥ 75 years), race (African-American, other), marital status (married, other), education [≤ high school versus

(vs.) more than high school], living situation (alone, other), and Body Mass Index (BMI) [≥ 19 vs. <19].

Cancer and treatment variables: We dichotomized cancer type as breast vs. other because a majority of participants had breast cancer; stage as I–II vs. III–IV; and receipt of surgery as Yes /No.

Comorbidity: We ascertained from medical records and also from self-report patients' comorbidities at study entry and used this information to calculate comorbidity count and the Charlson Comorbidity Index[31] for each participant.

Geriatric variables: We evaluated functional status using the following: Katz Activities of Daily Living (ADL), no dependency vs. ≥ one dependency; Lawton's Instrumental Activities of Daily Living (IADL), no dependency vs. ≥ one dependency; Eastern Cooperative Oncology Group Performance Status (ECOG-PS), 0–1 vs. ≥ 2; and Karnofsky Index of Performance Status (KPS), ≥ 80% vs. ≤ 70%. Patient self-report of falls in the last six months (0–1 vs. ≥ 2) was used to evaluate falls risk. The Vulnerable Elders Survey (VES-13) was used to assess risk of functional decline within 12 months (scores 0–2 vs. 3–10), with higher scores predicting increasing vulnerability. Cognitive status was evaluated with the Mini-Mental Status Examination (scores ≤ 23 vs. 24–30), with a score ≤ 23 indicating the possible presence of cognitive impairment.[32] Psychological/emotional state was assessed with the Geriatric Depression Scale (scores > 5 vs. ≤ 5), with scores > 5 indicating the possible presence of depression. Visual and hearing impairment were ascertained using a five-point Likert scale question. The Medical Outcomes Study Social Support Survey[33] was used to measure perceived social support. Participants scoring in the lowest quartile were assigned to the "perceived suboptimal social support" group vs. other. Finally, we developed a composite variable, geriatric deficits, defined as the presence of ≥ 1 deficit on any of the following assessments: MMSE, GDS, hearing and visual questionnaire, and MOS social support survey. We dichotomized geriatric deficits as 0–1 vs. ≥ 2, in order to identify participants with multiple deficits on the aforementioned screening tools. We did not include functional disability or multiple comorbidities in the geriatric deficit variable because we wanted to independently evaluate the association between functional status and comorbidity, and our outcomes of interest.

Data Analysis—We conducted descriptive analysis to examine participants' baseline characteristics. We classified the total number of medications taken by participants by each drugs' physiologic system of action (cardiovascular, respiratory, hematologic, endocrine, gastrointestinal, genitourinary, central nervous system, non-prescribed and miscellaneous) and used proportions to examine their distribution. We dichotomized all baseline characteristics and compared their distribution by polypharmacy and use of Beers Criteria Medication (*Yes or No*), using chi-squared tests.

Before performing linear/logistic regression analysis to identify correlates, we examined for highly co-linear variables among the functional status measures including ADL, IADL, ECOG-PS, KPS, and VES-13 scores using Spearman correlation. The five functional status variables were highly correlated with each other. ECOG-PS and KPS appeared to be better overall measures based on their correlations with all the other measures. ECOG and KPS were also very highly inter-correlated (r=−0.93), and we thus arbitrarily selected ECOG-PS as the measure of functional status to be used in univariate and multivariable linear and logistic regression analyses, see Table 1.

Next, using univariate linear regression analysis with medication count as a continuous outcome variable, we identified explanatory variables that had significant *($p \leq 0.05$)*

univariate linear associations with medication count. For explanatory variables that were categorical (sex, race, marital status, educational level, living situation, cancer type, stage, and receipt of surgery), dummy variables were created for use in all linear regression models. Using stepwise multiple linear regression analysis with medication count as the outcome variable and significant explanatory variables from univariate linear regression analysis, we identified factors that remained significantly and independently associated with medication count. Because the distribution of medication used was approximately normally distributed, we opted to use the more appropriate approach of linear regression methods that model the number of medications as a continuous outcome rather than logistic regression methods which are based on dichotomizing the outcome with an arbitrary cut-point. In these analyses, the regression coefficients are interpreted as the difference in mean number of medications between each category and the referent category for categorical explanatory variables, or the amount that the mean number of medications changes per unit increase of a continuous explanatory variable.

Lastly, to identify explanatory variables that were associated with Beers Criteria Medication count (dichotomized as none vs. ≥ 1), univariate logistic regression analyses were first undertaken. Then, using stepwise multiple logistic regression analysis with Beers Criteria Medication count as the outcome variable and significant explanatory variables from univariate logistic regression analysis, we identified factors that remained independently associated with Beers Criteria Medication count at the multivariate level. We chose to analyze Beers Criteria Medication count as a categorical variable rather than a continuous variable because a large proportion of the cohort were either prescribed none or just one medication, with very few being prescribed more than one. Explanatory variables were analyzed as continuous or as dummy variables.

All analyses were conducted using SAS version 9.1 (SAS institute, Cary, NC).

RESULTS

Participants' baseline characteristics

117 patients were enrolled into this study with a mean age of 74.6 years (SD=6.9). Table 2 displays the distribution of baseline characteristics. The majority of the participants (56%) were between the ages of 65 and 74 years. The study population consisted predominantly of white Medicare-insured patients, about half of whom had more than a high school education (45%), were other than married (65%), and lived alone (42%). Most participants had breast cancer (59%), stage I–II disease (59%), and underwent surgery (70%).

Participants took a total of 856 total medications, 659 prescribed and 197 non-prescribed medications, at study entry. The mean number of medications used by participants was 7.3 +/− 3.4, range (0–18), [5.6 +/− 3.1 prescribed medications, range (0–14) and 1.7 +/− 1.6 non-prescribed medications, range (0–6)]. The prevalence of polypharmacy and PIM use were 80% and 41%, respectively. Drugs acting on the cardiovascular system (31%) and the central nervous system (13%), and non-prescribed medications (23%) were the most commonly used medications. A total of 56 prescriptions were inappropriately prescribed based on Beers Criteria, and constituted 8.5% of all prescribed medications. The mean number of PIMs used by participants was 0.5 +/− 0.6, range 0–3. The proportion of study participants who were prescribed 0, 1, 2 and ≥ 3 PIMs was 59%, 35%, 5% and 1%, respectively. The four most commonly prescribed Beers Criteria Medications were lorazepam (16%), non-steroidal anti-inflammatory agents (16%), iron (16%) and digoxin (13%).

Table 2 presents the results of bivariate analysis of outcomes (polypharmacy and PIM use) according to baseline characteristics. At baseline participants who took ≥ 5 concurrent medications compared with those who took < 5 concurrent medications were more likely to: have IADL disability (100% vs. 0%, *P*=0.007); score ≥ 3 on the VES-13 (88% vs. 12%, *P*=0.03); have ≥ 5 comorbidities (88% vs.11%, p= 0.04); and to be prescribed Beers Criteria Medication (92% vs. 8%, *P*=0.01). Participants who were prescribed ≥ one Beers Criteria medication compared with those who were not prescribed any Beers Criteria medication were more likely to have other types of cancer than breast cancer (54% vs. 46%, *P*=0.02) and to have BMI < 19 (100% vs. 0%, *P*=0.03).

Simple linear regression analyses identified five univariate factors associated with medication use, (see Table 3). Multiple linear regression analysis identified three variables that were independently associated with medication use, see Table 3. All three factors had a positive linear relation relationship with medication use. For each increase in the number of comorbidities by one, there was an associated increase in the use of medications by 0.48 (95% CI (0.23, 0.73)); for each increase in ECOG-PS score by one, there was an associated increase in the use of medications by 0.79 (95% CI (0.18, 1.40)); and lastly for each increase in the number of Beers Criteria medication use by one, there was an associated increase in the use of medications by 1.22 (95% CI (0.37, 2.08)).

Table 4 presents results of univariate and multiple logistic regression analysis to identify factors associated with PIM use. The odds of using Beers Criteria Medications (PIMs) decreased by 10% for one unit increase in BMI [Odds Ratio (OR) 0.90, 95% CI = (0.84, 0.97)], and increased by 18% for each increase in medication count by one [OR 1.18, 95% CI = (1.04, 1.34)].

Discussion

In this cohort of patients, 65 years and older, with newly diagnosed cancer we found a very high prevalence of polypharmacy, and sometimes, medications being used were inappropriate. Participants with multiple comorbidities, sub-optimal performance status and on inappropriate medications were most likely to be on five or more concurrent medications. Factors associated with inappropriate medication use included having multiple comorbidities and being underweight.

The average use of 7.3 medications by our study participants is consistent with existing literature. Among older patients without a diagnosis of cancer, the average number of concurrent medication use, irrespective of whether non-prescribed medications are included in the medication count or not, have generally ranged from 3–8 medications. [1, 24, 28] However, there is a dearth of studies in older patients with cancer. Riechelmann et al.[14] found that oncology patients were receiving a median of five prescribed medications, however, the study population was not limited to the elderly population and had a median age of 58 years. Additionally, patients were all receiving systemic chemotherapy at time of study entry, which limits comparison to our study. Sokol et al.[27] found that geriatric oncology patients were receiving an average of nine prescribed and non-prescribed medications, but again, patients in this study were all receiving chemotherapeutic agents at time of study entry. The higher average in the Sokol et al.[27]study as compared to our study is likely due to the increasing number of medications required in patients actively undergoing chemotherapy.

Prevalence rates of polypharmacy in non-cancer patients have ranged from 5% to 78%.[34] The prevalence of polypharmacy (80%) in our study is slightly higher and concerning. Polypharmacy leads to an increased risk of drug-drug interaction, which could lead to

ADEs, particularly in patients receiving chemotherapy. This is especially of importance in the geriatric oncology population considering the altered pharmacokinetics, such as altered absorption, and renal and hepatic dysfunction. Given the known difficulties with medication management in the geriatric population and the complexities of polypharmacy in patients with malignancy, care should be taken to minimize the number of concurrent medications patients may be taking prior to and during cancer treatment.

Our study found an association between medication use and ECOG-PS scores, with patients taking multiple medications more likely to have poorer performance status. Prior studies in the older population, not directed toward the unique geriatric oncology population, have found conflicting results between polypharmacy and functional status in the elderly.[11, 12, 35] Agostini et al. examined the relationship between number of medications and weight loss or impaired balance in community-dwelling older adults, and found that for each increase in medication number, there was an increase in the likelihood of weight loss and impaired balance, even after controlling for confounding variables such as number of chronic diseases. [11] Weiner et al. found that the use of multiple central nervous system medications led to enhanced falls liability compared to the use of one central nervous system agent in community-dwelling older adults.[12] Lai et al. also found that polypharmacy correlated with an increased risk for hip fracture in the elderly population, while Pugh et al. found that polypharmacy was associated with decrements in lower extremity functional limitation.[35, 36] Studies examining the drug burden index (DBI), an evidence-based tool measuring a patient's exposure to sedative and anticholinergic medications, have found that a higher DBI score is independently associated with impairment in physical function, such as walking speed, IADLs, and Timed Up and Go (TUG) test.[37]

Poor functional status may be secondary to side effects of these medications and drug-drug interactions that result when polypharmacy is present. In addition poor functional status may be due to the presence of multiple comorbidities in many of these patients. Optimal functional status is especially important in the older adult with newly diagnosed cancer, as patients with poor functional status are at increased risk of toxicity with chemotherapeutic agents and increased mortality[38]. Multi-dimensional interventions that target the cluster of polypharmacy, multiple comorbidities and functional status may improve treatment tolerance and ultimately translate into improved cancer outcomes for older adults with cancer. Studies in this area are therefore warranted.

To the best of our knowledge only one prior published study has examined inappropriate prescribing of medications in older cancer patients. Using Beers Criteria, Flood et al.[15]found a prevalence rate of PIM use of 21% in geriatric oncology patients, in contrast to our study, which found a prevalence rate of 42%. However, patients in this study were not newly diagnosed but were acutely ill cancer patients hospitalized at study entry, which differs from our outpatient patient population. One reason our patient population may have had a higher prevalence rate of PIM use is that newly diagnosed patients with cancer, particularly in the post-surgical period, may require pain medications such as NSAIDS and anxiolytics such as benzodiazepines. Despite the high prevalence of PIM use in our study, it is important to note that a majority were prescribed only one PIM and only six percent of the entire study population was prescribed more than one PIM. Additionally, the most common PIMs prescribed to patients in this study (lorazepam, non-steroidal anti-inflammatory agents, iron and digoxin) are not known to have any adverse drug interactions with commonly used chemotherapeutic agents. Given that very few participants were on multiple PIMs and given the low likelihood of chemotherapy drug interactions with PIMs that were commonly used by our study participants, the adverse impact of PIM use in this population is likely to be minimal.

Previous studies regarding inappropriate prescribing of medications and functional status have also showed conflicting results, and were performed in the general elderly population and not specific to patients with cancer. [10, 35] Pugh et al. found that while polypharmacy was associated with impairment in lower extremity physical function, there was no association after controlling for confounding variables.[35] Hanlon et al. also found that there was no association between use of "drugs-to-avoid" and decline in functional status.[10] A higher DBI score has been independently associated with impairment in physical function.[37] In our study, PIM use was not directly associated with performance status. However, PIM use was associated with low BMI or being underweight. This finding is consistent with existing literature.[11] Low BMI may reflect reduced functional reserve among participants using PIMs. Weight loss is one of the key components of frailty[39] and is associated with health status decline, morbidity and mortality.[40, 41]

Our study has a number of limitations. First, the study was a single-institution study with a small sample size, albeit larger than the only two original studies in the geriatric oncology population. However, the consistency of our results with prior studies supports the robustness of our results. Second, the majority of the study population was mainly females with breast cancer, limiting the wide applicability of the study. However, sensitivity analyses limiting analysis to non-breast cancer patients only did not change our study conclusions. Third, the reliance on patient self-report and medical records for medication review rather than centralized pharmacy records may have led to underestimation of polypharmacy in this patient population. Fourth, the study is limited by the lack of information regarding the rationale for prescribing PIM. If a patient was found to be on a PIM, we were unable to ascertain if the patient was on the medication because they had failed safer alternatives or if no alternative medication existed for that patient. Avoidance of polypharmacy and PIM must be balanced with the necessity to treat patients with comorbid conditions, however, care should be taken to minimize the use of PIM when possible. Finally, the study is limited by a lack of evaluation of adverse drug reactions, a particularly pertinent issue in oncology given the potential for drug-drug interactions.

Further areas of exploration include interventions to decrease the frequency of polypharmacy and inappropriate prescribing. Given that polypharmacy and PIM use do not occur in isolation but in the context of functional disability and multi-morbidity, we recommend an approach of completing a CGA in all patients 65 years and older with newly diagnosed cancer and the establishment of a multi-disciplinary team to intervene on problems identified. This team should include a geriatric oncology pharmacist to help care providers identify potentially harmful medications and to decrease the number of medications that a patient is taking prior to initiation of chemotherapeutic regimens. In prior studies of patients without a diagnosis of cancer, a consultation by a pharmacist or a multidisciplinary panel has been found to be a proven beneficial strategy[42–44]. Hanlon et al. found that clinical pharmacists providing pharmaceutical care for elderly primary care patients can reduce inappropriate prescribing and possibly adverse drug effects[45]. This was also found to be cost-effective in elderly outpatients in a study by Cowper et al.[46] In patients with a diagnosis of cancer, Flood et al. found that the use of an interdisciplinary team in an acute care elders unit led to the discontinuation of PIM in 28% of the study population, however, studies are currently pending to determine if a correlative decrease in ADEs occurs.[15]

In conclusion, polypharmacy and inappropriate prescribing of medications were highly prevalent in this population of older patients with newly diagnosed cancer. Concurrent use of medication use was associated with functional disability and multi-morbidity whilst PIM use was associated with being underweight. CGA-driven interventions that target high-risk older cancer patients with the cluster of functional disability, multi-morbidity, and

polypharmacy/inappropriate medication use, may improve performance status, decrease frailty, and improve treatment tolerance among older patients with newly diagnosed cancer. This approach may ultimately translate to improved cancer outcomes for older adults and are therefore warranted.

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Table 1

Inter-correlation Between Functional Status Measures

	ADL	IADL	ECOG-PS	KPS	VES-13
	r†	r	r	r	r
Variables	p*	p	p	p	p
ADL	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _
IADL	0.59 <.0001	_ _ _	_ _ _	_ _ _	_ _ _
ECOG-PS	−0.62 <.0001	−0.74 <.0001	_ _ _	_ _ _	_ _ _
KPS	0.63 <.0001	0.79 <.0001	−0.93 <.0001	_ _ _	_ _ _
VES-13	−0.44 <.0001	−0.71 <.0001	0.68 <.0001	−0.70 <.0001	_ _ _

† r = Spearman correlation coefficient

* p = p-value

Activities of Daily Living (ADL); Instrumental Activities of Daily Living (IADL); Eastern Cooperative Oncology Group Performance Status (ECOG-PS); Karnofsky Performance Status (KPS); Vulnerable Elders Survey (VES)

Table 2

Bivariate Association Between Baseline Characteristics and Polypharmacy and Beers Criteria Medication Use

		Polypharmacy			Beers Criteria Medication		
		< 5	≥ 5		Yes	No	
Baseline Characteristics	**117 (100%)**	**23 (20%)**	**94 (80%)**	**p-value**	**48 (41%)**	**69 (59%)**	**p-value**
Demographics							
Age, Years							
65–74	65 (56)	12 (18.46)	53 (81.54)		27 (42)	38 (58)	
≥ 75	52 (44)	11 (21.15)	41 (78.85)	0.72	21 (40)	31 (60)	0.90
Sex							
Female	97 (83)	21 (21.65)	76 (78.35)		40 (41)	57 (59)	
Male	20 (17)	2 (10.00)	18 (90.00)	0.36	8 (40)	12 (60)	0.92
Race							
African-American	39 (33)	8 (20.51)	31 (79.49)		19 (49)	20 (51)	
Other	78 (67)	15 (19.23)	63 (80.77)	0.87	29 (37)	49 (63)	0.23
Marital Status							
Married	39 (35)	6 (15.38)	33 (84.62)		13 (33)	26 (67)	
Other	74 (65)	15 (20.27)	59 (79.73)	0.53	33 (45)	41 (55)	0.25
Missing	4						
Education							
High School or below	60 (54)	10 (16.67)	50 (83.33)		23 (38)	37 (62)	
Higher Level Education	52 (46)	11 (21.15)	41 (78.85)	0.54	23 (44)	29 (56)	0.53
Missing	5						
Living Situation							
Alone	48 (42)	9 (18.75)	39 (81.25)		22 (46)	26 (54)	
Other	65 (58)	12 (18.46)	53 (81.54)	0.97	24 (37)	41 (63)	0.34
Missing	4						
Cancer/Treatment Variables							
Cancer Type							
Breast	69 (59)	17 (24.64)	52 (75.36)		22 (32)	47 (68)	
Other	48 (41)	6 (12.50)	42 (87.50)	0.10	26 (54)	22 (46)	**0.02**
Stage							

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		Polypharmacy			Beers Criteria Medication		
		< 5	≥ 5		Yes	No	
Baseline Characteristics	**117 (100%)**	**23 (20%)**	**94 (80%)**	**p-value**	**48 (41%)**	**69 (59%)**	**p-value**
I–II	67 (59)	15 (22.39)	52 (77.61)		24 (36)	43 (64)	
III–IV	47 (41)	8 (17.02)	39 (82.98)	0.48	22 (47)	25 (53)	0.24
Missing	3						
Surgery							
Yes	81 (70)	18 (22.22)	63 (77.78)		30 (37)	51 (63)	
No	35 (30)	5 (14.29)	30 (85.71)	0.33	18 (51)	17 (49)	0.15
Missing	1						
Geriatric Variables							
ECOG-PS							
0–1	84 (72)	19 (22.62)	65 (77.38)		34 (40)	50 (60)	
2–4	33 (28)	4 (12.12)	29 (87.88)	0.20	14 (42)	19 (58)	0.85
Falls in the last six months							
0–1	107 (94)	21 (19.63)	86 (80.37)		44 (41)	63 (59)	
≥2	7 (6)	1 (14.29)	6 (85.71)	>0.999	3 (43)	4 (57)	>0.999
Missing	3						
VES-13 Scores							
0–2	52 (44)	15 (28.85)	37 (71.15)		18 (35)	34 (65)	
3–10	65 (56)	8 (12.31)	57 (87.69)	**0.03**	30 (46)	35 (54)	0.21
Comorbidity Count							
0–4	64 (55)	17 (26.56)	47 (73.44)		24 (38)	40 (62)	
≥5	53 (45)	6 (11.32)	47 (88.68)	**0.04**	24 (45)	29 (55)	0.39
Geriatric Deficits *							
0–1	73 (62)	15 (20.55)	58 (79.45)		29 (40)	44 (60)	
≥ 2	44 (38)	8 (18.18)	36 (81.82)	0.76	19 (43)	25 (57)	0.71
Miscellaneous Variables							
Body Mass Index							
< 19	4 (3)	0 (0.00)	4 (100.00)		4 (100)	0 (0)	
≥ 19	113 (97)	23 (20.35)	90 (79.65)	0.31	44 (39)	69 (61)	**0.03**

		Polypharmacy			Beers Criteria Medication		
		< 5	≥ 5		Yes	No	
Baseline Characteristics	**117 (100%)**	**23 (20%)**	**94 (80%)**	**p-value**	**48 (41%)**	**69 (59%)**	**p-value**
Beers Criteria Medication Use							
Yes	48 (41)	4 (8.33)	44 (91.67)		---	---	
No	69 (59)	19 (27.54)	50 (72.46)	0.01	---	---	

* Definition includes dementia, depression, visual and hearing impairments, and inadequate social support but excludes polypharmacy, functional disability and multiple comorbidities

Eastern Cooperative Oncology Group Performance Status (ECOG-PS); Vulnerable Elders Survey (VES-13)

Table 3

Results of Univariate and Multiple Linear Regression Analyses to Identify Predictors of Polypharmacy

	Univariate Linear Regression Analyses** Dependent Variable = Total Medication Count (continuous variable)			Multiple Linear Regression Dependent Variable = Total (continuous variable)		
Baseline Characteristics	**Regression coefficient**	**95% CI**	**P-value**	**Regression coefficient**	**95% CI**	**P-value**
Socio-Demographic Variables						
Age, Years	0.06	(−0.03, 0.15)	0.18			
Sex						
Female	**Referent**					
Male	0.61	(−1.06, 2.27)	0.47			
Race						
Other	**Referent**					
African-American	−0.64	(−2.00, 0.67)	0.34			
Marital Status						
Other	**Referent**					
Married	−0.55	(−1.88, 0.78)	0.42			
Education						
High School or below	**Referent**					
Higher Level Education	0.42	(−0.86, 1.70)	0.51			
Living Situation						
Other	**Referent**					
Alone	0.59	(−0.69, 1.88)	0.36			
Cancer Type						
Other	**Referent**					
Breast	−1.13	(−2.39, 0.13)	0.08			
Stage						
III–IV	**Referent**					
I–II	−0.67	(−1.96, 0.63)	0.31			
Surgery						
No	**Referent**					
Yes	−1.42	(−2.71, −0.10)	**0.04**			
Chemotherapy						

	Univariate Linear Regression Analyses** Dependent Variable = Total Medication Count (continuous variable)			Multiple Linear Regression Dependent Variable = Total (continuous variable)		
Baseline Characteristics	**Regression coefficient**	**95% CI**	**P-value**	**Regression coefficient**	**95% CI**	**P-value**
No	**Referent**					
Yes	−0.48	(−1.74, 0.78)	0.45			
ECOG-PS	**1.27**	**(0.64, 1.89)**	**0.0001**	**0.79**	**(0.18, 1.40)**	**0.006**
Falls in the last six months	0.53	(−0.27, 1.33)	0.20			
Comorbidity Count	**0.58**	**(0.33, 0.83)**	**<0.0001**	**0.48**	**(0.23, 0.73)**	**0.0002**
Geriatric Deficits *	**0.86**	**(0.37, 1.35)**	**0.0007**			
Body Mass Index	−0.03	(−0.12, 0.07)	0.59			
Beers Criteria Medication Use	**1.44**	**(0.49,2.40)**	**0.003**	**1.22**	**(0.36, 2.09)**	

*Definition includes dementia, depression, visual and hearing impairments, and inadequate social support but excludes polypharmacy, functional multiple comorbidities

**Explanatory variables were analyzed either as continuous or dummy variables

Eastern Cooperative Oncology Group Performance Status (ECOG-PS)

Table 4

Results of Univariate and Multiple Logistic Regression Analyses to Identify Predictors of Inappropriately Prescribed Medication Use

	Univariate Logistic Regression Analyses Dependent Variable = Beers Criteria Medication Count, *(Yes or No)*			Multiple Logistic Regression Analyses Dependent Variable = Beers Criteria Medication Count, *(Yes or No)*		
Baseline Characteristics	**Odds Ratio**	**95% CI**	**P-value**	**Odds Ratio**	**95% CI**	**P-value**
Socio-Demographic Variables						
Age, Years						
65–74	**Referent**					
≥ 75	0.99	(0.94, 1.04)	0.63			
Sex						
Female	**Referent**					
Male	0.95	(0.36, 2.54)	0.92			
Race						
Other	**Referent**					
African-American	1.61	(0.74, 3.49)	0.23			
Marital Status						
Other	**Referent**					
Married	0.62	(0.28, 1.39)	0.25			
Education						
High School or below	**Referent**					
Higher Level Education	0.78	(0.37, 1.67)	0.53			
Living Situation						
Other	**Referent**					
Alone	1.45	(0.68, 3.09)	0.34			
Cancer Type						
Other	**Referent**					
Breast	**0.40**	**(0.19, 0.85)**	**0.02**			
Stage						
III–IV	**Referent**					
I–II	0.63	(0.30, 1.36)	0.24			
Surgery						
No	**Referent**					

	Univariate Logistic Regression Analyses Dependent Variable = Beers Criteria Medication Count, *(Yes or No)*			Multiple Logistic Regression Analyses Dependent Variable = Beers Criteria Medication Count, *(Yes or No)*		
Baseline Characteristics	**Odds Ratio**	**95% CI**	**P-value**	**Odds Ratio**	**95% CI**	**P-value**
Yes	0.56	(0.25, 1.24)	0.15			
Chemotherapy						
No	**Referent**					
Yes	1.10	(0.52, 2.31)	0.80			
ECOG-PS						
0–1	**Referent**					
2–4	1.26	(0.85, 1.87)	0.25			
Falls in the last six months						
0–1	**Referent**					
≥ 2	1.24	(0.77, 2.00)	0.37			
Comorbidity Count						
0–4	**Referent**					
≥ 5	1.08	(0.92, 1.27)	0.32			
Geriatric Abnormalities						
0–1	**Referent**					
≥ 2	1.14	(0.84, 1.54)	0.39			
Body Mass Index						
≥ 19	**Referent**			**Referent**		
< 19	**0.90**	**(0.85, 0.97)**	**0.003**	**0.90**	**(0.84, 0.97)**	**0.003**
Polypharmacy						
< 5	**Referent**			**Referent**		
≥ 5	**1.18**	**(1.04, 1.33)**	**0.008**	**1.18**	**(1.04, 1.34)**	**0.009**

*Definition includes dementia, depression, visual and hearing impairments, and inadequate social support but excludes polypharmacy

**Explanatory variables were analyzed either as continuous or dummy variables

Eastern Cooperative Oncology Group Performance Status (ECOG-PS)