Published in final edited form as:
J Am Geriatr Soc. 2014 August ; 62(8): 1505–1512. doi:10.1111/jgs.12942.

Polypharmacy and Potentially Inappropriate Medication Use among Older Adults with Cancer Undergoing Chemotherapy: Impact on Chemotherapy-Related Toxicity and Hospitalization During Treatment

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Abstract

Polypharmacy and potentially inappropriate medication (PIM) use are understudied among older adults with cancer undergoing chemotherapy. The current study's aims were to evaluate in this

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Manuscript writing: All authors
Final approval of manuscript: All authors

Meetings: An abstract of this study was accepted and presented at the Annual Meeting of the American Society of Clinical Oncology on June 3, 2013 (abstract 9545).

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

population: 1) the prevalence of polypharmacy and PIM use; and 2) the association between these and chemotherapy-related adverse events.

Methods—This was a secondary analysis of prospectively collected data of adults age ≥65 years with cancer undergoing chemotherapy. Measures included: the number of daily medications (i.e, polypharmacy); PIM use based on 3 indices [Beers, Zhan, and Drugs to Avoid in the Elderly (DAE) criteria], as well as use of 6 "high-risk" medication classes for adverse drug events (i.e., anticoagulants, antiplatelet agents, opioids, insulin, oral hypoglycemics and antiarrhythmics). Using multivariate logistic regression, the relations were evaluated between these criteria and 1) Grade 3-5 chemotherapy-related toxicity; and 2) hospitalization during chemotherapy.

Results—The patients (N=500; mean age, 73 years, 61% Stage IV disease) took a mean of 5 daily medications (±4; range, 0-23). PIM use among patients was common (up to 29% using Beers criteria). No association was found between the number of daily medications and either toxicity (0-3 medications as reference: 4-9, OR=1.34, 95% CI: 0.92-1.97; ≥10, OR=0.82, 95% CI: 0.45-1.49), or hospitalization (0-3 medications as reference, ≥4, OR=1.34, 95%CI: 0.82-2.18, p=0.24). There was also no association between PIM use and toxicity (p=0.93) or hospitalization (p=0.98). No medication class was associated with either outcome.

Conclusions—Polypharmacy and PIM use were common but werenot associated with chemotherapy-related toxicity or hospitalization in older adults with cancer.

Keywords

Polypharmacy; Cancer; Elderly; Chemotherapy; Toxicity

INTRODUCTION

Polypharmacy is a common problem in the general geriatric population.[1, 2] Depending on definitions used and study design, the prevalence of polypharmacy among older adults in the outpatient setting can be up to 37%,[3-5] and up to 92% among those who are hospitalized.[6, 7]Polypharmacy can increase the potential for clinically significant drug-drug interactions and can ultimately lead to increased risk of adverse drug events, increased health resource utilization, decreased quality of life, and increased morbidity, including falls and hospitalization.[8-10]

Polypharmacy may be an even more important consideration for older adults with cancer. This is especially important to study as patients 65 years and older now represent the largest proportion of newly diagnosed patients with cancer in the United States.[11]These patients may be more vulnerable to the adverse effects of polypharmacy than older adults without cancer, as they are typically exposed to both chemotherapy-specific drugs as well as other related medications that may increase the risk of adverse drug events. These adverse events can include chemotherapy-related toxicity. For example, use of anticoagulant agents and chemotherapy-related thrombocytopenia or the concurrent use of warfarin with fluorouracil may increase the risk for bleeding. Furthermore, many older adults with cancer have multiple comorbid conditions, which may require multiple medications for health maintenance.[12, 13] The National Institute of Aging and the National Cancer Institute have

highlighted that medication use in older adults with cancer is an underexplored area of research.[14]

Several important knowledge gaps exist related to polypharmacy and PIM use in older adults in general. First, although multiple methods exist to assess for polypharmacy and PIM use, very few studies have incorporated more than one approach to evaluate them in older adults.[15, 16] One approach is counting the number of medications (prescription, non-prescription, or both) concomitantly taken by a patient. A limitation of this approach is that it fails to capture medication "appropriateness", which is important, since heterogeneity exists among drugs in their risk for causing adverse drug events as well as their potential for clinical benefit. Consequently, several indices have been created and validated to identify potentially inappropriate medication (PIM) use, including the Beers criteria[17], the Zhan criteria[18], and the DAE list.[19]Consequently, the use of some medications for supportive care purposes such as benzodiazepines and anticholinergics for nausea may be considered PIM use, which may increase risk for toxicity. Furthermore, specific medication classes (e.g., anticoagulants) in older adults have been associated with increased risk of adverse drug events precipitating hospitalization.[20, 21] Although several studies have evaluated some components of polypharmacy and PIM use in older adults with cancer, their association with adverse clinical outcomes remains undefined.[22-24] Thus, little is known about the clinical impact they might have on older adults with cancer receiving chemotherapy.

The goal of the current study was to address these knowledge gaps in a large cohort of older adults with cancer undergoing chemotherapy. First, the prevalence of polypharmacy and PIM use was assessed. Second, the association between medication measures (i.e., polypharmacy, PIM use, and high-risk medication classes) and adverse events during chemotherapy (i.e., chemotherapy-related toxicity and hospitalization during treatment) was evaluated.

METHODS

Study Design

We conducted a secondary analysis of data derived from a multi-center, prospective, longitudinal study evaluating the role of a pre-treatment comprehensive geriatric assessment (CGA) in a cohort of older adults with cancer undergoing chemotherapy (N=500).[25] Eligible patients consisted of individuals aged 65 years or older who carried a diagnosis of any type of solid-tumor malignancy (excluding non-melanoma skin cancer); were about to receive outpatient chemotherapy as part of their cancer treatment; were English-speaking; and were able to provide informed consent. Institutional review board approval had been obtained at all participating sites.

Measures

Patients completed a baseline CGA, which evaluated several functional and psychosocial domains including: comorbidity type and number; recent history of falls (within prior 6 months); recent history of unintentional weight loss (within prior 6 months); activities of daily living (ADL) and self-reported physical function; instrumental activities of daily living

(IADL); cognitive function; mood; self-reported social function and social support; Karnofsky performance status (KPS), and routine laboratory data. The details of the CGA used, including the domain measures, monitoring, and follow-up details have previously been described.[25, 26]

Patients provided a list of all medications currently being taken. This included all prescription and non-prescription agents being taken either on a scheduled or on an as-needed basis. Reported medication lists were subsequently verified with those found in the medical record and reconciled by the treating physician and the site's study team. Specific aspects of medication administration, such as dosage and frequency, were not included *a priori* as part of the original assessment.

Several standardized approaches to evaluate polypharmacy and PIM use were incorporated. First, the numbers of overall and prescription-only medications were measured and analyzed separately. Second, potentially inappropriate medication (PIM) use was measured using the following 3 validated indices: 1) the 2012 Beers criteria[17]; 2) the Zhan criteria[18]; and 3) the 2011 DAE list.[19] The Beers criteria comprise a list of medications deemed inappropriate for use in older adults based on a risk-benefit ratio. They are divided into two components: drugs/drug classes considered inappropriate for any older adult and drugs/drug classes that may be inappropriate based on the presence of a specific coexisting illness. Given known limitations of the data regarding comorbid conditions recorded, only the first component of the Beers criteria was applied. Similarly, medications rendered inappropriate due to a specific dosage or frequency were also excluded, since this information was not captured *a priori*. In addition, any medication listed as having "strong anticholinergic properties" in the Beers criteria was also deemed inappropriate.[27]

Although considered otherwise as "inappropriate" by the Beers criteria, the following drugs were encountered in the study cohort, with 12% taking at least 1 agent: lorazepam, prochlorperazine, metoclopramide, and atropine/diphenoxylate. Given this low prevalence, lack of specific indication, and that such agents are typically used to ameliorate chemotherapy-induced nausea (lorazepam, prochlorperazine, metoclopramide) or diarrhea (atropine/diphenoxylate), the study group had reached a consensus determining that they not be rendered "inappropriate" *per se*. Therefore, the analysis was performing both including and excluding these four agents.

Both the Zhan criteria and the DAE list are derivations of the Beers criteria. The Zhan criteria contain an abbreviated list of potentially inappropriate medications prescribed for the elderly patient, subcategorized as follows: those drugs that *should always be avoided*; those that *should rarely be used*; and those that are *sometimes indicated*. Conversely, the DAE list consists solely of a modified first component of the Beers criteria. Finally, in addition to these PIM measures, 6 high-risk medication classes were also evaluated, consisting of anticoagulants, antiplatelet agents, insulins, oral hypoglycemics, opioids, and antiarrhythmics since they have been identified with a higher risk of adverse drug events precipitating hospitalization in older adults.[20, 21]

Analyses

Descriptive statistics (mean, standard deviation (SD), range, frequencies) were calculated to examine the baseline patient characteristics. Unconditional logistic regression analyses were used to evaluate the association between medication measures (i.e., number of daily medications, PIM use, use of the 6 high-risk medication classes), and the likelihood of an adverse chemotherapy-related event (presence or absence). Based on prior results showing the predictive ability of specific clinical and CGA factors for chemotherapy-related toxicity in this cohort[25], the following covariates were evaluated as potential confounders: age; presence of gastrointestinal or genitourinary cancer type; use of empirically dose-reduced chemotherapy; use of polychemotherapy; hemoglobin level; renal function; presence of self-reported hearing impairment; history of falls; presence of self-reported mobility limitation (i.e., not able to walk one block without assistance); self-reported difficulty in self-administration of medications; and self-reported decreased social activity.

Number of daily medications was initially considered both categorically and continuously as anindependentvariable for the analysis. Since no consensus on a cut-off value for number of medications defining polypharmacy exists, data-driven Lowess curves were generated to assess the relationship between number of daily medications and chemotherapy-related toxicity and hospitalization, respectively. The first curve demonstrated 2 inflection points, identifying 3 distinct daily medication number subgroups: 0-3, 4-9, and ≥10 daily medications. The second curve revealed 1 significant inflection point (0-3 vs. ≥4 medications). Similar exploratory data analyses were also used for number of prescription medications, revealing that number of prescription medications had a linear relationship with both outcomes, and thus could be treated continuously in the analysis.

PIM use was dichotomized as present or absent (yes =1 vs. no=0) for each PIM index individually as well as for *any* index (i.e., Beers criteria, Zhan criteria, DAE list). Use of high-risk medications was similarly treated. Chemotherapy-related toxicity was defined as any grade 3 or higher toxicity as determined by the National Cancer Institute's Common Terminology Criteria for Adverse Events (version 3.0).[28] In general, grade 3 toxicity is a severe adverse event, grade 4 is a disabling or life-threatening adverse event, andgrade 5 is a death related to an adverse event. Hospitalization rates were determined by a record of ≥1 hospitalization during the chemotherapy treatment course.

For the bivariate analysis, the association between the independent variables (polypharmacy, PIM use, and CGA measures) and dependent variables (chemotherapy-related outcome measures) were analyzed by Wald chi-square analysis or Fisher's exact test, where appropriate. Similarly, continuous dependent variables were analyzed by the modified student's t-test. Covariates that might serve as potential confounders were evaluated by ascertaining ≥15% change from the crude to the adjusted odds ratio in each analysis of number of daily medications and a given outcome. For the association between number of daily medications and chemotherapy-related toxicity, no confounders were identified. However, for the association between number of daily medications and hospitalization risk, creatinine clearance and comorbidity number (categorized as <2 vs. ≥2) were identified as confounders and thus included in the final model. To check for interactions between each of

these confounders and the number of daily medications and their association with hospitalization risk, thelikelihood ratio test was performed. Neither the interaction with comorbidity nor that with creatinine clearance was found to be statistically significant and therefore these interaction terms were not included in the final analysis. All statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC) and STATA SE 12.0 (StataCorp, College Station, TX).

RESULTS

The CGA was completed by 500 older patients with cancer scheduled to receive chemotherapy. All patients had sufficient medication and toxicity data for analysis. The majority of the patients were 70 years or older; were female; and had advanced lung or gastrointestinal cancers (Table 1). Patients were followed for a median time of 79days (range, 6-598 days) from the time of study enrollment to either treatment completion or treatment discontinuation due to progression of disease, excessive toxicity, or patient choice.

Number of Medications

Patientstook a mean of 5 daily medications (SD 4; range, 0-23), with an overall mean of 7 (SD 4; range, 0-25) (daily + as-needed). The frequency of prescription medication use was similar to that of daily medication use in general (mean 4; SD 3; range, 0-20).

PIM Use

Based on the drug-class component of the 2012 Beers criteria, 147 (29%) of the 500 patients were taking at least 1 inappropriate medication. Of these at-risk patients, 37 (25%) were receiving 2 or more inappropriate medications. The 3 most commonly used inappropriate drugs identified were zolpidem (5%), alprazolam (4%), and propoxyphene (2%). Based on the Zhan criteria, 54 (11%) patients were on at least 1 inappropriate medication, with 3 of thesepatients receiving 2 such medications, for a total of 57 inappropriate medications being used. Five of these medications were categorized as “should be avoided”; 28 as “should rarely be used”; and 24 as “sometimes indicated.” Based on the DAE list, 69 (13%) patients were taking at least 1 inappropriate medication, with 6of these patients taking 2 such medications, for a total of 75 inappropriate medications being used. Propoxyphene, which has since been removed from the US market in late 2010, was the most frequently encountered potentially inappropriate medication utilizing the Zhan and DAE criteria (data not shown).

Polypharmacy, PIM Use, and Association with Chemotherapy-Related Adverse Events

Overall, 265 (53%) patients experienced any Grade 3-5 chemotherapy-related toxicity (Grade 3: 39%; Grade 4, 26%; Grade 5, 2%). Specifically, 132 (26%) patients experienced Grade 3 or higher hematologic toxicity, whereas 217 (43%) experienced Grade 3 or higher non-hematologic toxicity. There was no significant association between number of daily medications and chemotherapy-related toxicity (Table 2). Specifically, using 0-3 daily medications as the reference group, increasing the number of daily medications did not increase the likelihood of chemotherapy-related toxicity (4-9 daily medications, OR=1.34, 95% CI: 0.92-1.97, P=0.13; ≥10, OR=0.82, 95% CI: 0.45-1.49, P=0.51). Overall, 115 (23%)

patients were hospitalized during chemotherapy. There was no significant association between the number of daily medications and hospitalization after adjusting for potential confounders [creatinine clearance and comorbidity number (categorized as <2 vs. ≥2)] (Table 3). The number of prescription medications and the total number of medications (i.e., daily and as-needed) medications, were also not associated with an increased risk of either chemotherapy-related outcome (data not shown). The presence of PIM use defined by the 2012 Beers Criteria was not found to be an independent predictor of chemotherapy toxicity (Table 2);similar findings were found for the presence of any PIM use regardless of the index applied (Appendix). Furthermore, these results did not change whether or not the definition of PIM use included the four supportive care medications (atropine/diphenoxylate, lorazepam, metoclopramide, and prochlorperazine), which are commonly used in oncology practice (data not shown). PIM use was also not associated with a higher risk of hospitalization during chemotherapy (Table 3; Appendix). However, a borderline statistically significant association was identified between anticoagulant use and an increased risk for chemotherapy-related toxicity (P=0.05) (Table 2).

DISCUSSION

Medication use was prevalent among our study cohort of older adults with cancer. We identified a mean of 5 daily and 7 total medications per patient, consistent with smaller prior outpatient-based geriatric oncology-specific studies,[23, 24] yet lower than those values seen in an inpatient setting.[22, 29] These modest differences are likely attributable to variation in study design, including operational definitions of polypharmacy and potential differences in coexisting comorbid conditions, with higher numbers potentially indicating increased prevalence.[30] However, our analysis of older adults with cancer undergoing therapy may be more robust since it was derived from a larger cohort than previously reported studies (N=500 vs. N=47 to 405).

Potentially inappropriate medication (PIM) use was also common. Utilizing the 2012 Beers criteria, we found a higher prevalence of PIM use (29%) than with the 2003 version (17%, data not shown). The latter value was comparable to that found in studies evaluating the 2003 version in geriatric oncology-based studies (11-21%).[22, 23] Further geriatric oncology-based studies utilizing the 2012 criteria are therefore needed. By applying the Zhan criteria and the 2011 DAE list, we found a prevalence of 11% and 13%, respectively. To our knowledge, prior studies have not yet applied these indices to a geriatric oncology population. However, in general geriatric outpatient-based populations, the prevalence of PIM use according to these criteria ranges from 16% to 20%, with these values mostly derived from claims-based data.[4, 31, 32]

Although polypharmacy and PIM use were common in our cohort, they were not associated with chemotherapy-related toxicity outcomes among this cohort. Rather, CGA factors previously identified remain stronger predictors of toxicity.[25] Although increased number of comorbid conditions is associated with an increased likelihood of polypharmacy,[24, 33] comorbidities, were not over-represented in the patients who had a chemotherapy-related adverse outcome, with no interactions detected in our analysis (data not shown). Even by including six high-risk medication classes that have been associated with an increased risk

for hospitalization among older adults, we did not find such association with increased risk of hospitalization during the chemotherapy course. It is possible that there are more complex interactions at work that our secondary analysis could not identify. Perhaps utilizing different or a combination of distinct criteria, we would have encountered different results, since alternative metrics, such as the Medication Appropriateness Index (MAI), can capture medications more accurately associated with risk for adverse drug events.[34, 35] Moreover, polypharmacy and PIM use are linked to several other non-chemotherapy-related adverse outcomes that are just as clinically important such as non-chemotherapy adverse drug reactions and potential for functional decline and falls, which portend significant morbidity in older adults and were not captured in our study.[21, 36]

We acknowledge that our study has several limitations. First, the evaluation of polypharmacy and PIM use was a cross-sectional, secondary analysis, which might not have sufficiently been powered to detect more modest effect size differences. Second, we performed our analysis utilizing only overall Grade 3-5 hematologic and non-hematologic chemotherapy-related toxicities as the outcome and did not explore the potential association with individual specific toxicities or specific reasons for hospitalization. Finally, we did not include other components of medication use (i.e., indication, dosage, and frequency), which may be clinically important and are an essential part of other criteria such as the MAI; or criteria that provide more clinical examples by which one can render a medication inappropriate or to avoid medication duplication such as the STOPP criteria.[37] Given these considerations, the true prevalence of polypharmacy and PIM use may be higher and begins to approach that seen in inpatient or frail elderly settings.[6, 7, 10] There is a challenge of evaluating polypharmacy and PIM use that may not rest solely in the paucity of data in older adults with cancer, but also in the inherent ambiguity surrounding its definition. As evidenced by this study, there are potentially medications or combinations of medications that may be appropriate for a given older patient with cancer to help support him or her through chemotherapy. As a result, we feel this study highlights the need for the development of geriatric oncology-centric definitions of polypharmacy and PIMuse, given the complexity of clinical issues that arise in the study of older adults.[38]

Despite these limitations, our study's findings have shed light on the impact of polypharmacy and PIM use on two key outcomes in a geriatric oncology population. Our study builds upon prior work by incorporating multiple components of polypharmacy and PIM use, including the most updated version of the Beers criteria. In addition, several medications that are considered PIMs are used frequently as supportive care agents in older cancer patients, thus raising the question whether criteria should be modified to accommodate a geriatric oncology population. Perhaps most importantly, in a large sample of older adults with cancer receiving chemotherapy, we did not find an association between polypharmacy and a higher risk of either chemotherapy-related toxicity or hospitalization during treatment. However, polypharmacy and PIM use can still have a significant impact on other clinically important outcomes such as non-chemotherapy adverse drug reactions and falls not evaluated in our study. While this negative finding is somewhat reassuring, future prospective studies specifically designed to evaluate polypharmacy and PIM use in relationship with these and other clinical outcomes in a geriatric oncology population are needed.

Acknowledgments

Funding Sources:

This research was supported by K23 AG026749-01 - Paul Beeson Career Development Award in Aging Research (PI: Dr. Hurria), and American Society of Clinical Oncology--Association of Specialty Professors--Junior Development Award in Geriatric Oncology (PI: Dr. Hurria). Dr. Maggiore's efforts are supported by T32 AG19134 (National Institute on Aging geriatric research training grant) under the guidance of Drs. Gross, Hurria, and Thomas Gill. Dr. Dale's efforts are supported by John A. Hartford Center of Excellence in Geriatrics. Dr. Gross's efforts are supported by 1 K08 AG24842 (Paul Beeson Career Development Award in Aging Research).

The authors would like to thank Drs. Andrew Chapman, Harvey Cohen, June McKoy, Hy Muss, and the rest of the CARG members for their ongoing feedback and support throughout the course of the study.

Sponsor's Role: The sponsor had no role in the design or conduct of the study.

Appendix

Association between Other PIM measures and grade 3-5 Chemotherapy-Related Toxicity

Variables	Toxicity N (%)	No Toxicity N (%)	OR (95% CI)	P value
PIM use: Zhan criteria				
Absent	235 (53)	209 (47)	Reference group	
Present	29 (54)	25 (46)	1.03 (0.59-1.82)	0.91
PIM use: DAE				
Absent	230 (53)	200 (47)	Reference group	
Present	35 (51)	34 (49)	0.90 (0.54-1.49)	0.67
PIM use: Any PIM use				
Absent	186 (53)	164 (47)	Reference group	
Present	78 (53)	70 (47)	0.98 (0.67-1.44)	0.93

Abbreviations: CI: confidence interval; DAE, Drugs to Avoid in the Elderly list; OR, odds ratio; PIM, potentially inappropriate medication(s).

Association between Other PIM measures and Hospitalization during Chemotherapy

Variables	Hospitalized N (%)	Not Hospitalized N (%)	OR (95% CI)	P value
PIM use: Zhan criteria				
Absent	105 (24)	339 (77)	Reference group	
Present	9 (17)	45 (83)	0.64 (0.31-1.37)	0.25
PIM use: DAE				
Absent	103 (24)	327 (77)	Reference group	
Present	12 (17)	57 (83)	0.67 (0.35-1.29)	0.23
PIM use: Any PIM use				
Absent	80 (23)	270 (77)	Reference group	
Present	34 (23)	114 (77)	1.01 (0.64-1.59)	0.98

Abbreviations: CI: confidence interval; DAE, Drugs to Avoid in the Elderly list; OR, odds ratio; PIM, potentially inappropriate medication(s).

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Table 1

Baseline Patient Characteristics

Patient Characteristic	N (% Total)	Patient Characteristic	N (% Total)
Age*		**Medication Intake** (OARS scale)*	
≥72 years*	270 (54)	No assistance	461 (92)
<72 years	230 (46)	Requires assistance*	39 (8)
Gender		**Falls in Past 6 months***	
Female	281 (56)	0	407 (81)
Male	219 (44)	≥1*	91 (18)
		Missing	2 (0)
Race/Ethnicity		**Self-Reported Hearing***	
Caucasian	426 (85)	Excellent/Good	370 (74)
African-American	42 (8)	Fair/Poor/Deaf*	123 (25)
Asian	26 (5)	Missing	7 (1)
Other	6 (1)		
Education Level		**Creatinine Clearance** (mL/min)*	
Less than High School	18 (4)	≥34 (Jelliffe/IBW)	440 (88)
High School Graduate	175 (35)	<34(Jelliffe/IBW)*	44 (9)
Associate's/Bachelor's Degree	306 (61)	Missing	16 (3)
Graduate/Professional Degree	104 (21)		
Missing	1 (0)		
Living Situation		**Hemoglobin (g/dL)***	
Lives Alone	106 (21)	≥10 (female)/ ≥11 (male)	429 (86)
Lives with Spouse/Family Member	390 (78)	<10 (female)/ <11 (male)*	62 (12)
Missing	4 (1)	Missing	9 (2)
Employment Status		**Limited in Walking 1 block** (MOS scale)*	
Employed (Full- or Part-Time)	83 (17)	Not limited at all	386 (77)
Retired/Homemaker/Unemployed	395 (79)	Limited*	109 (22)
Disabled/Medical Leave	21 (4)	Missing	5 (1)
Missing	1 (0)		
Cancer Stage		**Decreased Social Activity** (MOS scale)*	
I-II	82 (17)	A little/None of the Time	278 (56)
III	109 (22)	Some/Most/All of the Time*	218 (44)
Limited Stage	2 (0)	Missing	4 (0)
Stage IV/Extensive Stage	307 (61)		
Cancer Type*		**Empiric Chemotherapy Dose Reduction***	

Patient Characteristic	N (% Total)	Patient Characteristic	N (% Total)
Lung	143 (29)	No	380 (76)
GI*	135 (27)	Yes*	120 (24)
Gyn	87 (17)		
Breast	57 (11)		
GU*	50 (10)		
Other	28 (6)		
Physician-Rated KPS (%)		**No. of Chemotherapy Agents***	
>70	402 (80)	Single Agent	149 (30)
≤70	86 (18)	Multiple Agents*	351 (70)
Missing	12 (2)		

Abbreviations: GI: Gastrointestinal; GU: Genitourinary; Gyn: Gynecologic; IBW: Ideal Body Weight; KPS, Karnofsky Performance Status; MOS, Medical Outcomes Study; OARS, Older Americans Resources and Services;

*Significant GA predictors of chemo toxicity in older adults with cancer (Hurria et al. JCO 2011)

Table 2

Association between Medication Measures and Grade 3-5 Chemotherapy-Related Toxicity

Variables	Toxicity N (%)	No Toxicity N (%)	OR (95% CI)	P value
Number of daily medications				
Continuous	----	----	1.01 (0.96-1.06)	0.85
Number of daily medications				
0-3	91 (50)	92 (50)	Reference group	
4-9	141 (57)	106 (43)	1.34 (0.92-1.97)	0.13
≥10	25 (45)	31 (55)	0.82 (0.45-1.49)	0.51
PIM use: Beers 2012				
Absent	181 (53)	160 (47)	Reference group	
Present	77 (52)	70 (48)	0.97 (0.66-1.43)	0.89
Use of high-risk medications: Anticoagulants				
No	236 (52)	221 (48)	Reference group	
Yes	29 (67)	14 (33)	1.94 (1.00-3.77)	0.05
Use of high-risk medications: Antiplatelets				
No	204 (54)	174 (46)	Reference group	
Yes	61 (50)	61 (50)	0.85 (0.57-1.28)	0.45
Use of high-risk medications: Antiarrhythmics				
No	249 (53)	224 (47)	Reference group	
Yes	16 (59)	11 (41)	1.31 (0.59-2.88)	0.50
Use of high-risk medications: Opioids				
No	206 (54)	179 (46)	Reference group	
Yes	59 (51)	56 (49)	0.92 (0.60-1.39)	0.68
Use of high risk-medications: Oral Hypoglycemics				
No	244 (54)	209 (46)	Reference group	
Yes	21 (45)	26 (55)	0.69 (0.38-1.27)	0.23
Use of high-risk medications: Insulin				
No	258 (53)	226 (47)	Reference group	
Yes	7 (44)	9 (56)	0.68 (0.25-1.86)	0.45

Abbreviations: CI: confidence interval; OR, odds ratio; PIM, potentially inappropriate dedication.

Table 3

Association between Medication Measures and Hospitalization during Chemotherapy

Variables	Hospitalized N (%)	Not Hospitalized N (%)	OR (95% CI)	P value
Number of daily medications				
0-3	31 (17)	152 (83)	Reference group	
≥4	81 (27)	222 (73)	1.34 (0.82-2.18)[1]	0.24
PIM use: Beers 2012				
Absent	76 (22)	265 (78)	Reference group	
Present	33 (22)	114 (78)	1.01. (0.64-1.61)	0.97
Use of high-risk medications: Anticoagulants				
No	103 (23)	354 (78)	Reference group	
Yes	12 (28)	31 (72)	1.33 (0.66-2.68)	0.43
Use of high-risk medications: Antiplatelets				
No	85 (23)	293 (78)	Reference group	
Yes	30 (25)	92 (75)	1.12 (0.70-1.81)	0.63
Use of high-risk medications: Antiarrhythmics				
No	105 (22)	368 (78)	Reference group	
Yes	10 (37)	17 (63)	2.06 (0.92-4.64)	0.08
Use of high-risk medications: Opioids				
No	91 (24)	294 (76)	Reference group	
Yes	24 (21)	91 (79)	0.85 (0.51-1.42)	0.54
Use of high-risk medications: Oral Hypoglycemics				
No	101 (22)	352 (78)	Reference group	
Yes	14 (30)	33 (70)	1.48 (0.76-2.87)	0.25
Use of high-risk medications: Insulin				
No	109 (23)	375 (77)	Reference group	
Yes	6 (38)	10 (62)	2.68 (0.73-5.81)	0.17

[1] Adjusted for creatinine clearance and comorbidity number (categorized as <2 vs. ≥2).

Abbreviations: CI, confidence interval; OR, odds ratio; PIM, potentially inappropriate medication(s).